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Dkt No. : 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 1

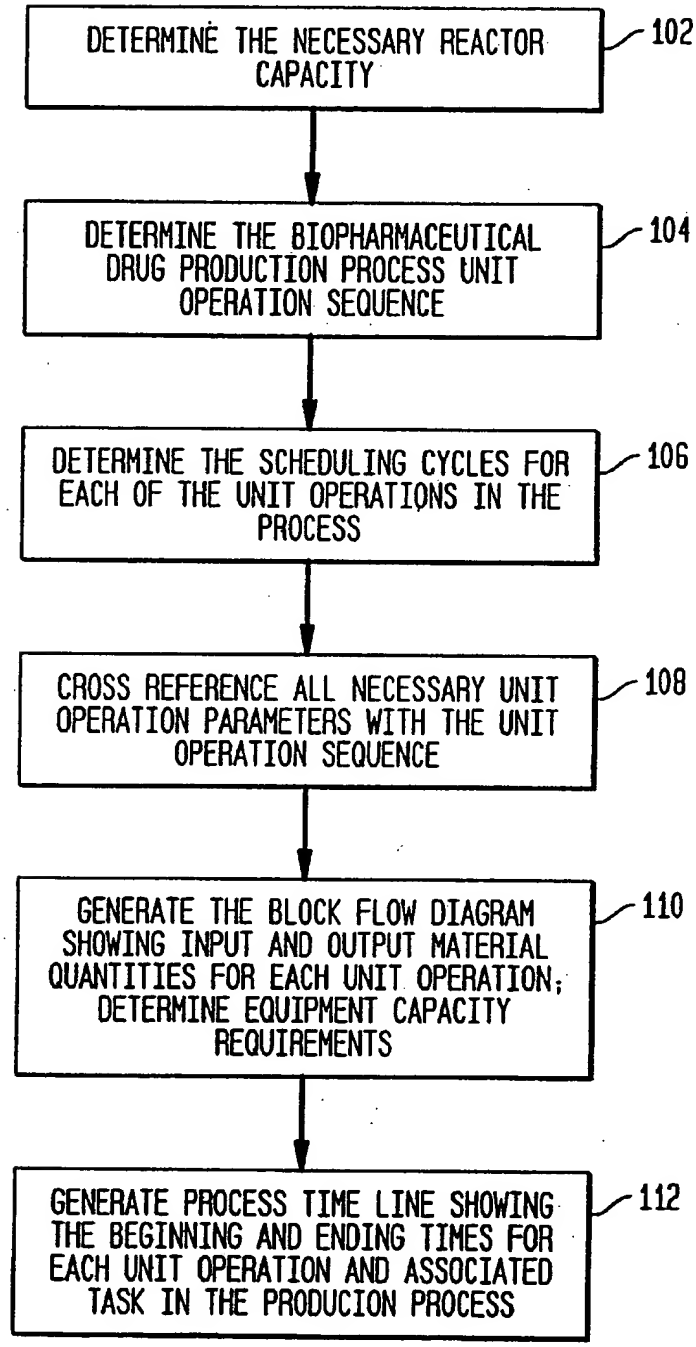

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FIG. 2

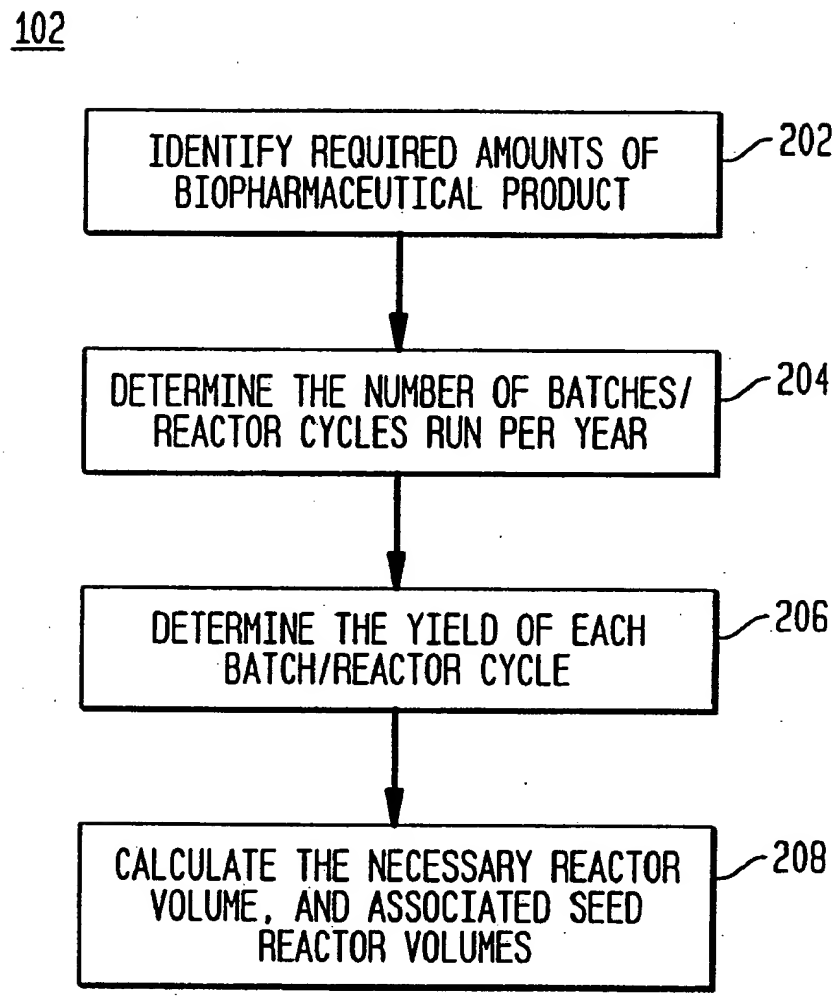

FIG. 3
UNIT OPERATIONS LIST

MICROBIAL FERMENTATION PROCESS

UOP SEQ. NO.	CODE	UNIT OPERATION TYPE	CYCLES PER									RECOVERY			
			UnOp		BATCH				PROCESS						
				OFFSET (HRS)		UnOp START	UnOp END	OFFSET (HRS)		UnOp START	UnOp END	OFFSET (HRS)	PRODUCT		TOTAL PROTEIN	
													SWR	OAR	SWR	OAR
1	1	INOCULUM PREP	1		3	1	6		1							
2	2	FLASK GROWTH	1		3	1	6		1							
3	53	SEED FERMENTATION	1		3	1	6		1							
4	3	PRODUCTION FERMENTATION	1		3	1	6		1				100%	100%	100%	100%
5	51	HEAT EXCHANGE	1		3	1	6		1				100%	100%	100%	100%
6	28	CONT. CENTRIFUGATION/WHOLE CELL HARVEST	1		3	1	6		1				95%	95%	95%	95%
7	48	RESUSPEND CELL PASTE	1		1				1				100%	95%	100%	95%
8	51	HEAT EXCHANGE	1		3	8	10		1				100%	95%	100%	95%
9	31	CELL DISRUPTION/HIGH PRESSURE	1		3	8	10		1				80%	76%	90%	86%
10	51	HEAT EXCHANGE	1		3	8	10		1				100%	76%	100%	86%
11	48	RESUSPENSION/SURFACTANT	1		2	11	12		1				100%	76%	95%	81%
12	29	CONT. CENTRIFUGATION/PRECIPITATE HARVEST	1		2	11	12		1				95%	72%	32%	26%
13	48	RESUSPENSION/BUFFER	1		1				1				100%	72%	95%	24%
14	29	ULTRAFILTRATION/CONCENTRATION/DILUTION	1		1				1				95%	69%	95%	23%
15	48	MICROFILTRATION/TANGENTIAL FLOW	1		1				1				93%	64%	95%	22%
16	36	PRODUCT ADSORPTION HPLC	1		1				1				85%	54%	33%	7%
17	34	PRODUCT ADSORPTION HPLC	1		1				1				90%	49%	40%	3%
18	39	ULTRAFILTRATION/FLOW DIALYSIS	1		1				1				95%	46%	95%	3%
19	39	PRODUCT ADSORPTION HPLC	1		1				1				85%	39%	55%	2%
20	37	ULTRAFILTRATION/FLOW DIALYSIS	1		1				1				90%	35%	95%	1%
21	39	PRODUCT ADSORPTION HPLC	1		1				1				90%	32%	80%	1%
22	37	MICROFILTRATION/DEAD END	1		1				1				95%	30%	95%	1%
23	99	END														
			302	304	306	308	310	312	314	316	318	320	322	324	326	328	330	332

Replacement Sheet
Sheet 3 of 167
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FIG. 4
UNIT OPERATIONS LIST

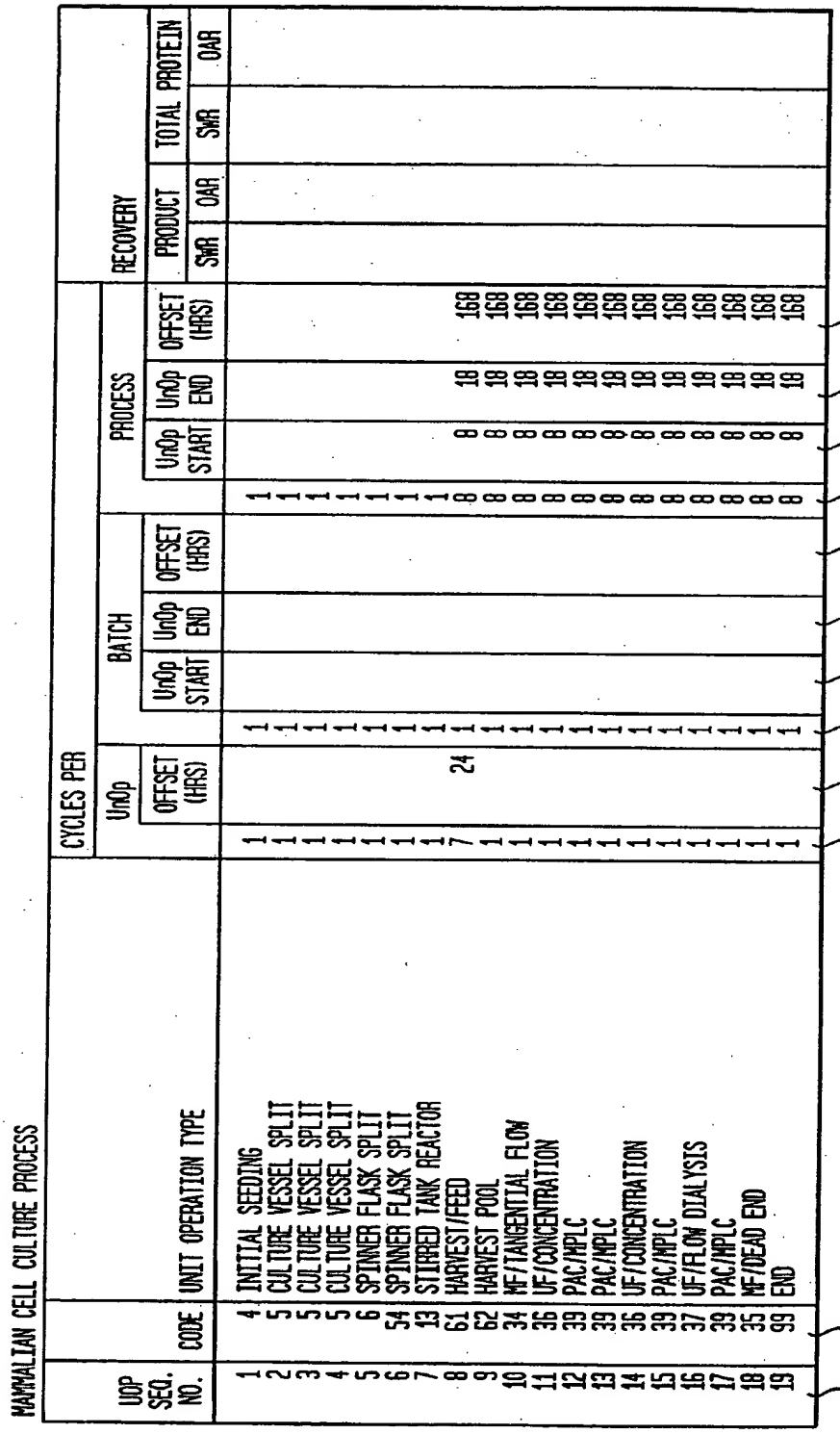
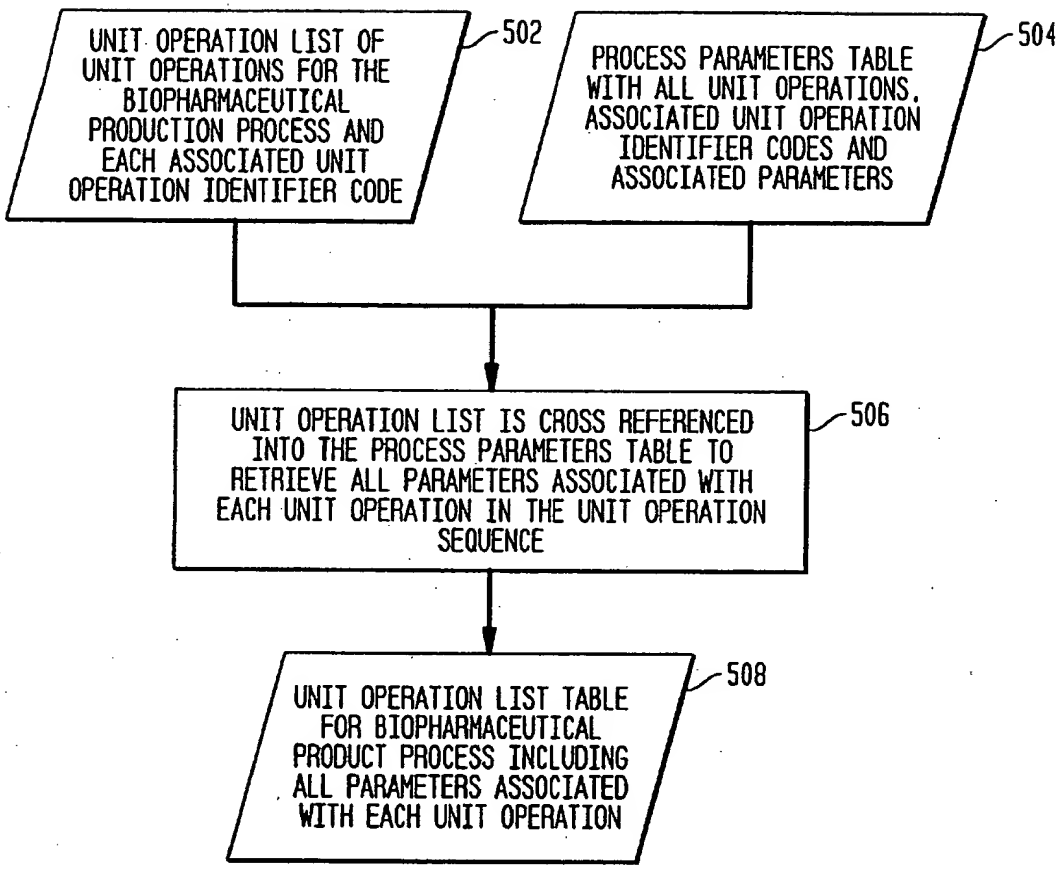


FIG. 5


UNIT OPERATION LIST OF UNIT OPERATIONS FOR THE BIOPHARMACEUTICAL PRODUCTION PROCESS AND EACH ASSOCIATED UNIT OPERATION IDENTIFIER CODE
502
PROCESS PARAMETERS TABLE WITH ALL UNIT OPERATIONS, ASSOCIATED UNIT OPERATION IDENTIFIER CODES AND ASSOCIATED PARAMETERS
504
UNIT OPERATION LIST IS CROSS REFERENCED INTO THE PROCESS PARAMETERS TABLE TO RETRIEVE ALL PARAMETERS ASSOCIATED WITH EACH UNIT OPERATION IN THE UNIT OPERATION SEQUENCE
506
UNIT OPERATION LIST TABLE FOR BIOPHARMACEUTICAL PRODUCT PROCESS INCLUDING ALL PARAMETERS ASSOCIATED WITH EACH UNIT OPERATION
508

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(As Amended)

FIG. 6A

UNIT OPERATION ID CODE	UNIT OPERATION TYPE	PARAMETERS
1	INOCULUM PREP	# OF FLASKS, VOLUME OF FLASKS, TEMPERATURE, AGITATION, DURATION, FINAL OD
2	FLASK GROWTH	SCALE UP RATIO, MEDIA VOLUME, TEMPERATURE, AGITATION, DURATION, FINAL OD
3	FERMENTATION SEED	SCALE UP RATIO, FERMENTOR WORKING VOLUME, ANTIFOAM, BASE ACID, GROW TEMPERATURE, AGITATION, SPARGE RATE, BACK PRESSURE, TOTAL DURATION
4	FERMENTATION PRODUCTION	SCALE UP RATIO, GERMENTOR WORKING VOLUME, ANTIFOAM A, ANTIFOAM B, BASE, ACID, GROW TEMPERATURE, AGITATION, SPARGE RATE, BACK PRESSURE, TOTAL DURATION, FINAL OK, DRY CELL MASS, PRODUCT CONCENTRATION, CIP, SIP
5	HEAT EXCHANGE	PROCESS INITIAL & FINAL TEMP; UTILITY INITIAL & FINAL TEMP; PROCESS SPECIFIC HEAT; DESIGN TYPE, STEP RECOVERY OF PRODUCT, STEP RECOVERY OF T.P., TEMPERATURE REGULATION, CIP, SIP
6	BATCH CENTRIFUGATION	SYSTEM VOID VOLUME, RCF, TIME, VOLUME REDUCTION, WASH VOLUME, CLEAN, RINSE
7	RESOLUBLIZATION RESUSPENSION	REAGENT/PRODUCT RATIO, TITRATION SOLUTION, RESOLUBLIZATION, AGITATION, SOLUTION NAME, STEP RECOVERY OF THE PRODUCT, STEP RECOVERY OF T.P., TEMPERATURE REGULATION, CIP, SIP
8	CELL DISRUPTION HIGH PRESS. HOMOGENIZATION	PRODUCT TEMPERATURE, UNILITY TEMPERATURE, VOID VOLUME, NUMBER OF PASSES, PRESSURE, FLOW RATE, TEMPERATURE INCREASE, WASH, RINSE, STEP RECOVERY OF PRODUCT, STEP RECOVERY OF T.P., TEMPERATURE REGULATION, CIP
9	DILUTE WITH SURFACTANT	REAGENT PRODUCT RATIO, TITRATION SOLUTION, DILUTION TIME, AGITATION, SOLUTION NAME, STEP RECOVERY OF PRODUCT, STEP RECOVERY OF T.P., TEMPERATURE REGULATION, CIP, SIP
10	BATCH CENTRIFUGATION PRECIPITATE HARVEST	SYSTEM VOID VOLUME, RCF, TIME, VOLUME REDUCTION, WASH VOLUME, CLEAN, RINSE, STEP RECOVERY OF PRODUCT, STEP RECOVERY OF T.P., TEMPERATURE REGULATION, CIP, SIP
11	RESUSPEND WITH CHAOTROPE	REAGENT/PRODUCT RATIO, TITRATION SOLUTION, RESOLUBLIZATION, AGITATION, SOLUTION NAME, STEP RECOVERY OF PRODUCT, STEP RECOVERY TO TP, TEMPERATURE REGULATION, CIP, SIP
•	•	•
•	•	•
•	•	•
•	•	•

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FIG. 6B

504

SOLUTION TYPE	TASKS	TASK DURATION
S-101	SETUP, PREINCUBATION, INCUBATION, CLEAN UP	3, 3, 23, .3, HRS
S-101	SETUP, PREINCUBATION, INCUBATION, CLEAN UP	1, 1, 23, .3, HRS
S-101, 102, 103, 104, 105	SETUP, PREINCUBATION, FERMENTATION, HARVEST, CIP, SIP, CLEAN UP	1, 1, 21, .5, 1, 1, 3 HRS
S-101, 102 103, 104, 105	SETUP, PREINCUBATION, FERMENTATION, CIP, SIP, CLEAN UP	•
	SETUP, TRANSFER, CIP, SIP, CLEAN UP	•
S-106	SETUP, CENTRIFUGATION, WASH, CIP, SIP, CLEANUP	•
S-107	SETUP, DILUTION, AGITATE, CIP, SIP, CLEAN UP	•
S-107	SETUP, LYSIS, CIP, SIP, CLEAN UP	•
S-108	SETUP, DILUTION, AGITATE, CIP, SIP, CLEAN UP	•
S-108	SETUP, CENTRIFUGATION, WASH, CIP, SIP, CLEAN UP	•
S-109	SETUP, FLUSH, PRIME, CONCENTRATION, DILUTION, WASH, FLUSH, STORE, CIP, SIP, CLEANUP	•
•	•	•

• • •

FIG. 7

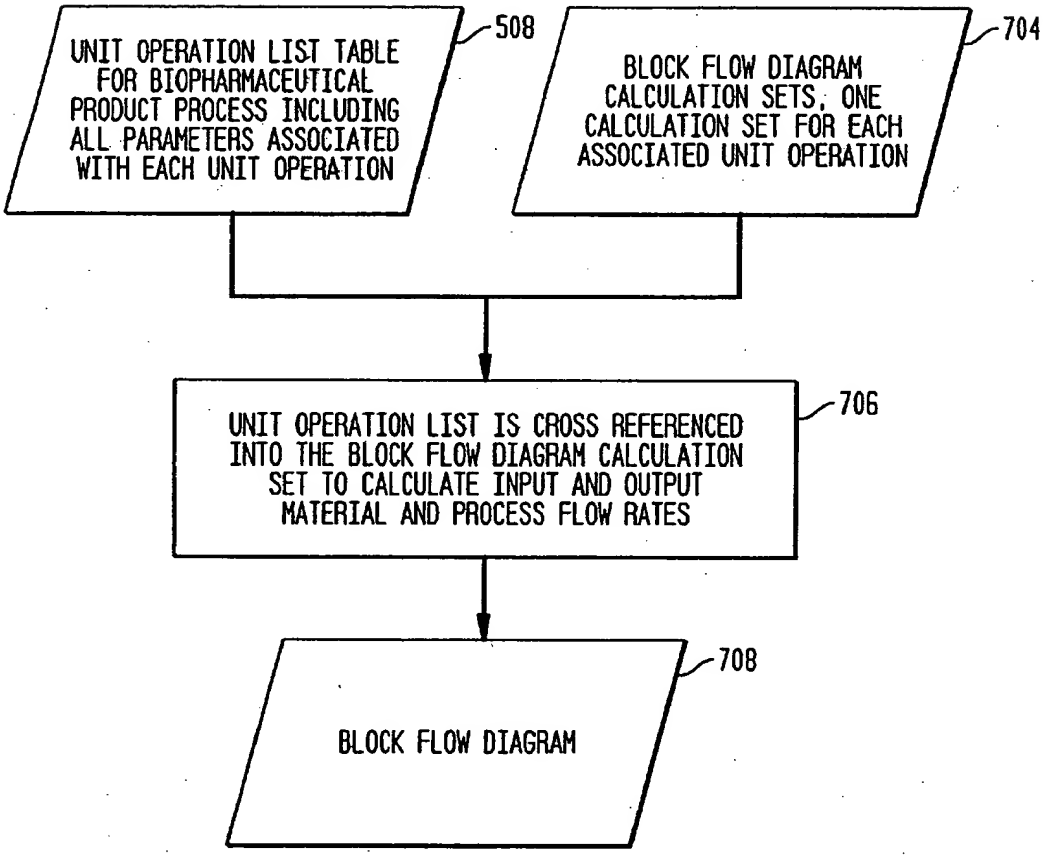
UNIT OPERATION LIST TABLE FOR BIOPHARMACEUTICAL PRODUCT PROCESS INCLUDING ALL PARAMETERS ASSOCIATED WITH EACH UNIT OPERATION
508
BLOCK FLOW DIAGRAM CALCULATION SETS, ONE CALCULATION SET FOR EACH ASSOCIATED UNIT OPERATION
704
UNIT OPERATION LIST IS CROSS REFERENCED INTO THE BLOCK FLOW DIAGRAM CALCULATION SET TO CALCULATE INPUT AND OUTPUT MATERIAL AND PROCESS FLOW RATES
706
BLOCK FLOW DIAGRAM
708

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FIG. 8

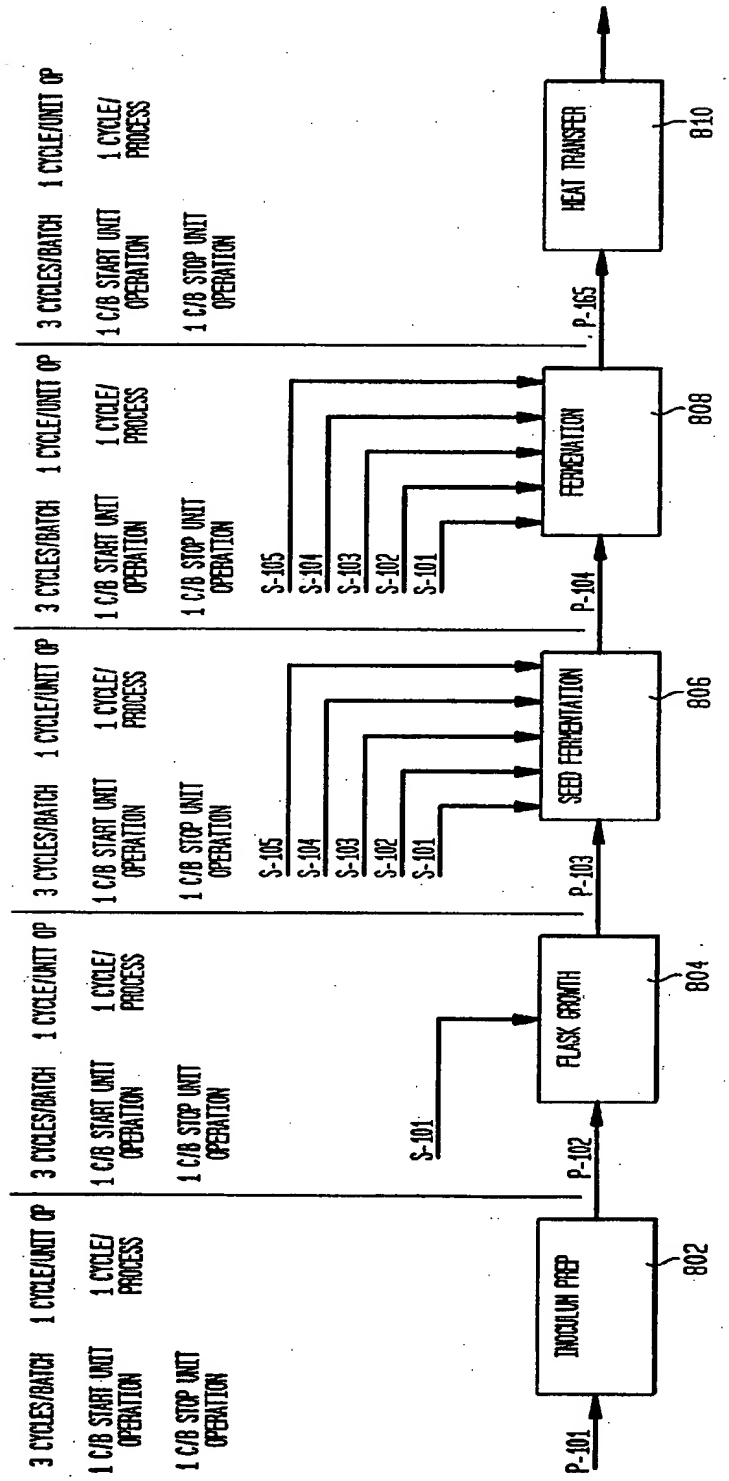

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FIG. 9

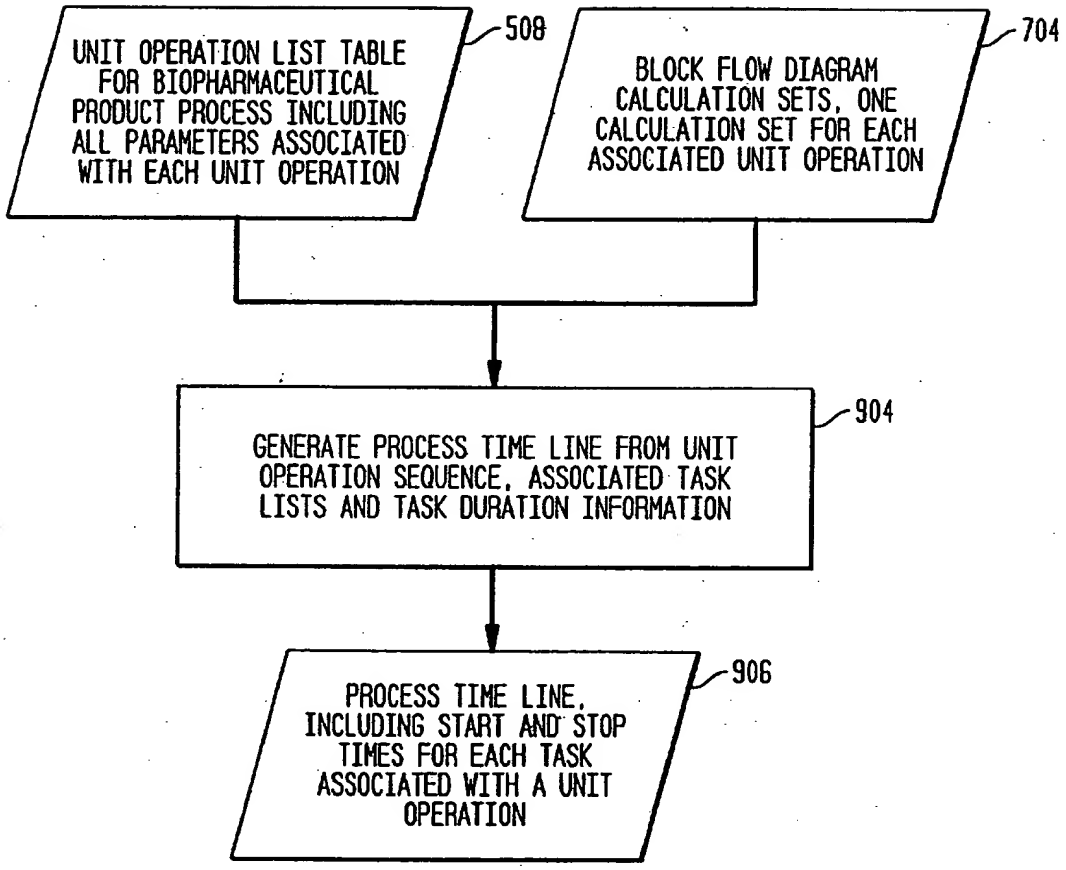

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FIG. 10

SAMPLE APPLICATION OF PROCESS DESIGN CYCLES IN PROCESS SCHEDULING

MICROBIAL FERMENTATION PROCESS (SEE UNIT OPERATION LIST)

			DURATION	FIRST PROCESS CYCLE WEEK	DAY	SECOND PROCESS CYCLE WEEK	DAY
NOTE: NONE OF THE UNIT OPERATIONS IN THIS PROCESS HAVE MORE THAT 1 CYCLE PER UNIT OPERATION (SEE UNIT OPERATION 8 IN THE MAMMALIAN CELL CULTURE PROCESS FOR AN EXAMPLE OF MULTIPLE CYCLES PER UNIT OPERATION)							
UNIT OPERATIONS 1-6 UNDERGO THREE REPETATIVE CYCLES PER BATCH AS A SET BEFORE CONTINUING WITH UNIT OP 7 THIS TRANSLATES TO THREE RUNS ON A FERMENTOR WITH EACH HARVEST (UNIT OP 5 & 6) BEING STORED FOR POOLING AT UNIT OP 7 ASSOCIATED WITH EACH FERMENTOR RUN (UNIT OP 4) ARE THE PREVIOUS STEPS FOR INNOCULATION PREP (UNIT OPS 1-3)							
1/3 FERMENTATION CYCLES PER BATCH							
	1	INOCULUM PREP	24 HRS	1 FRI - SAT		2 FRI - SAT	
	2	FLASK GROWTH	24 HRS	2 SAT - SUN		3 SAT - SUN	
	3	SEED FERMENTAION	24 HRS	2 SUN - MON		3 SUN - MON	
	4	PRODUCTION FERMENTATION	24 HRS	2 MON - TUE		3 MON - TUE	
	5	HEAT EXCHANGE	1 HR	2 TUE		3 TUE	
	6	CENTRIFUGATION	1 HR	2 TUE		3 TUE	
2/3 FERMENTATION CYCLES PER BATCH							
	1	INOCULUM PREP	24 HRS	2 SUN - MON		3 SUN - MON	
	2	FLASK GROWTH	24 HRS	2 MON - TUE		3 MON - TUE	
	3	SEED FERMENTAION	24 HRS	2 TUE - WED		3 TUE - WED	
	4	PRODUCTION FERMENTATION	24 HRS	2 WED - THU		3 WED - THU	
	5	HEAT EXCHANGE	1 HR	2 THU		3 THU	
	6	CENTRIFUGATION	1 HR	2 THU		3 THU	
3/3 FERMENTATION CYCLES PER BATCH							
	1	INOCULUM PREP	24 HRS	2 TUE - WED		3 TUE - WED	
	2	FLASK GROWTH	24 HRS	2 WED - THU		3 WED - THU	
	3	SEED FERMENTAION	24 HRS	2 THU - FRI		3 THU - FRI	
	4	PRODUCTION FERMENTATION	24 HRS	2 FRI - SAT		3 FRI - SAT	
	5	HEAT EXCHANGE	1 HR	2 SAT		3 SAT	
	6	CENTRIFUGATION	1 HR	2 SAT		3 SAT	
UNIT OPERATION 7 POOLS THE HARVESTS FROM THE THREE FERMENTATION CYCLES ABOVE							
	7	POOL HARVESTS	3 HR	3 MON		4 MON	
UNIT OPERATIONS 8-9 UNDERGO THREE REPETATIVE CYCLES PER BATCH AS SET BEFORE CONTINUING WITH UNIT OPERATION 11 THIS TRANSLATES TO THREE CONSECUTIVE PASSES THROUGH CELL DISRUPTOR (UNIT OP 9) WITH ITS ASSOCIATED HEAT EXCHANGERS (UNIT OP 8 & 10) AT THE INLET AND THE OUTLET OF THE CELL DISRUPTOR							
1/3 DISRUPTION CYCLES PER BATCH							
	8	HEAT EXCHANGE					
	9	CELL DISRUPTION					
	10	HEAT EXCHANGE	0.5 HR	3 MON		4 MON	
2/3 DISRUPTION CYCLES PER BATCH							
	8	HEAT EXCHANGE					
	9	CELL DISRUPTION					
	10	HEAT EXCHANGE	0.5 HR	3 MON		4 MON	
3/3 DISRUPTION CYCLES PER BATCH							
	8	HEAT EXCHANGE					
	9	CELL DISRUPTION					
	10	HEAT EXCHANGE	0.5 HR	3 MON		4 MON	

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FIG. 11

SAMPLE APPLICATION OF PROCESS DESIGN CYCLES IN PROCESS SCHEDULING

MICROBIAL FERMENTATION PROCESS (SEE UNIT OPERATION LIST)

			FIRST PROCESS CYCLE	SECOND PROCESS CYCLE
		DURATION	WEEK DAY	WEEK DAY
UNIT OPS 11-12 UNDERGO TWO REPETATIVE CYCLES PER BATCH AS A SET BEFORE CONTINUING WITH UNIT OP 13 THIS TRANSLATES TO TWO CYCLES OF RESUSPENDING THE CELL TYSATE FROM THE CELL DISRUPTOR IN A MILD SURFACTANT AND RECONCENTRATING THE INSOLUBLE PRODUCT TO A PASTE BY CENTRIFUGATION				
1/2 PRODUCT WASHING CYCLES PER BATCH				
11	RESUSPENSION	0.5 HR	3 MON	4 MON
12	CENTRIFUGATION	1 HR	3 MON	4 MON
2/3 PRODUCT WASHING CYCLES PER BATCH				
11	RESUSPENSION	0.5 HR	3 MON	4 MON
12	CENTRIFUGATION	1 HR	3 MON	4 MON
UNIT OPS 13-22 UNDERGO ONLY ONE CYCLE PER UNIT OPERATION EACH TO THE END OF THE PROCESS				
13	RESUSPENSION	0.5 HR	3 MON	4 MON
14	BUFFER EXCHANGE	2 HR	3 MON	4 MON
15	FILTRATION	2 HR	3 MON	4 MON
16	LIQUID CHROMATOGRAPHY	16 HRS	3 MON - TUE	4 MON - TUE
17	LIQUID CHROMATOGRAPHY	4 HRS	3 TUE	4 TUE
18	BUFFER EXCHANGE	2 HRS	3 TUE	4 TUE
19	LIQUID CHROMATOGRAPHY	2 HRS	3 WED	4 WED
20	BUFFER EXCHANGE	2 HRS	3 WED	4 WED
21	LIQUID CHROMATOGRAPHY	2 HRS	3 WED	4 WED
22	FILTRATION	2 HRS	3 WED	4 WED

FIG. 12A-1

	OPERATION	PROCESS TIME LINE													CALCULATIONS
		DURATION (HRS.)			REL. TIME SCALE (HRS)			ABS. DAYS		START		FINISH			
		CALC.	A/D	ADJ.	PREP	EXEC.	COMPL.	START	END	DATE	TIME	DATE	TIME		
						15.5				06/03/96	08:00 AM				
1	1 A INOCULUM PREP														
2															
3	SET UP	3.0	0.0	3.0 HRS	12.5			0.40	0.52	06/03/96	09:30 AM	06/03/96	12:30 PM		
4	PREINCUBATION	3.0	0.0	3.0 HRS	15.5			0.52	0.65	06/03/96	12:30 PM	06/03/96	03:30 PM		
5	INCUBATION	23.0	0.0	23.0 HRS		38.5		0.65	1.60	06/03/96	03:30 PM	06/04/96	02:30 PM		
6	CLEAN UP	0.3	0.0	0.3 HRS			38.8	1.60	1.61	06/04/96	02:30 PM	06/04/96	02:45 PM		
6	SUBTOTAL	29.0		29.0 HRS		38.5									
7															
8	2 A FLASK GROWTH														
9															
10	SET UP	1.0	0.0	1.0 HRS	37.5			1.52	1.56	06/04/96	12:30 PM	06/04/96	01:30 PM		
11	PREINCUBATION	1.0	0.0	1.0 HRS	38.5			1.56	1.60	06/04/96	01:30 PM	06/04/96	02:30 PM		
12	INCUBATION	23.0	0.0	23.0 HRS		61.5		1.60	2.56	06/04/96	02:30 PM	06/05/96	01:30 PM		
13	CLEAN UP	0.3	0.0	0.3 HRS			61.8	2.56	2.57	06/05/96	01:30 PM	06/05/96	01:45 PM		
13	SUBTOTAL	25.0		25.0 HRS		61.5									
14															
15	3 A SEED FERMENTATION														
16															
17	SET UP	1.0	0.0	1.0 HRS	60.5			2.48	2.52	06/05/96	11:30 AM	06/05/96	12:30 PM		
18	PREINCUBATION	1.0	0.0	1.0 HRS	61.5			2.52	2.56	06/05/96	12:30 PM	06/05/96	01:30 PM		
19	FERMENTATION	21.0	0.0	21.0 HRS		82.5		2.56	3.44	06/05/96	01:30 PM	06/06/96	10:30 AM		
20	HARVEST	0.5	0.0	0.5 HRS		83.0		3.44	3.46	06/06/96	10:30 AM	06/06/96	11:00 AM	50.0 L	1.7 LPM = 0.50 HRS
21	CIP	1.0	0.0	1.0 HRS			83.5	3.44	3.48	06/06/96	10:30 AM	06/06/96	11:30 AM		
22	SIP	1.0	0.0	1.0 HRS			84.5	3.48	3.52	06/06/96	11:30 AM	06/06/96	12:30 PM		
23	CLEAN UP	3.0	0.0	3.0 HRS			87.5	3.52	3.65	06/06/96	12:30 PM	06/06/96	03:30 PM		
24	SUBTOTAL	28.5		28.5 HRS		83.0									
25															

FIG. 12A-2

26	4 A PRODUCTION FERMENTATION														
27															
28	SET UP	1.0	0.0	1.0 HRS	82.5			3.38	3.42	06/06/96	09:00 AM	06/06/96	10:00 AM		
29	PREINCUBATION	1.0	0.0	1.0 HRS	83.0			3.42	3.46	06/06/96	10:00 AM	06/06/96	11:00 AM		
30	FERMENTATION	21.0	0.0	21.0 HRS		104.0		3.46	4.33	06/06/96	11:00 AM	06/07/96	08:00 AM		
31	CIP	1.0	0.0	1.0 HRS			105.0	4.33	4.38	06/07/96	08:00 AM	06/07/96	09:00 AM		
32	SIP	1.0	0.0	1.0 HRS			106.0	4.38	4.42	06/07/96	09:00 AM	06/07/96	10:00 AM		
33	CLEAN UP	2.0	0.0	2.0 HRS			108.0	4.42	4.50	06/07/96	10:00 AM	06/07/96	12:00 PM		
34	SUBTOTAL	27.0		27.0 HRS		104.0									
35															
36	5 A HEAT EXCHANGE														
37															
38	SET UP	0.50	0.0	0.5 HRS	104.5			4.33	4.35	06/07/96	08:00 AM	06/07/96	08:30 AM		
39	TRANSFER	1.00	0.0	1.0 HRS		105.0		4.33	4.38	06/07/96	08:00 AM	06/07/96	09:00 AM	562.1 LB	9.4 LPM = 1.00 HRS
40	CIP	1.0	0.0	1.0 HRS			106.0	4.38	4.42	06/07/96	09:00 AM	06/07/96	10:00 AM		
41	SIP	1.0	0.0	1.0 HRS			107.0	4.42	4.46	06/07/96	10:00 AM	06/07/96	11:00 AM		
42	CLEAN UP	2.0	0.0	2.0 HRS			109.0	4.46	4.54	06/07/96	11:00 AM	06/07/96	01:00 PM		
43	SUBTOTAL	5.0		5.0 HRS		105.0									
44															
45	6 A CONT. CENT./SOLIDS														
46															
47	SET UP	1.00	0.0	1.0 HRS	105.0			4.33	4.38	06/07/96	08:00 AM	06/07/96	09:00 AM		
48	CENTRIFUGATION	1.00	0.0	1.0 HRS		106.0		4.38	4.42	06/07/96	09:00 AM	06/07/96	10:00 AM	562.1 LB	9.4 LPM = 1.00 HRS
49	WASH	0.10	0.0	0.1 HRS		106.1		4.42	4.42	06/07/96	10:00 AM	06/07/96	10:06 AM	1.0 LB	0.2 LPM = 0.10 HRS
50	CIP	0.25	0.0	0.3 HRS			106.4	4.42	4.43	06/07/96	10:06 AM	06/07/96	10:21 AM	20.0 LB	1.3 LPM = 0.25 HRS
51	SIP	1.00	0.0	1.0 HRS			107.4	4.43	4.47	06/07/96	10:21 AM	06/07/96	11:21 AM		
52	CLEAN UP	0.50	0.0	0.5 HRS			107.9	4.47	4.49	06/07/96	11:21 AM	06/07/96	11:51 AM		
53	SUBTOTAL	3.85		3.85 HRS		106.1									
54															
55	1 B INOCULUM PREP														
56															
57	SET UP	1.0	0.0	1.0 HRS	14.5			0.56	0.60	06/03/96	01:30 PM	06/03/96	02:30 PM		
58	PREINCUBATION	1.0	0.0	1.0 HRS	15.5			0.60	0.65	06/03/96	02:30 PM	06/03/96	03:30 PM		
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15

Replacement Sheet
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Appl. No. : 09/100,088; Filed: June 19, 1998
Dkt No. : 1606.002004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 12B-1

	OPERATION	PROCESS TIME LINE												CALCULATIONS
		DURATION (HRS.)			REL. TIME SCALE (HRS)			ABS. DAYS		START		FINISH		
		CALC.	A/D	ADJ.	PREP	EXEC.	COMPL.	START	END	DATE	TIME	DATE	TIME	
						15.5				06/03/96	08:00 AM			
59	INCUBATION	23.0	0.0	23.0 HRS		38.5		0.65	1.60	06/03/96	03:30 PM	06/04/96	02:30 PM	
60	CLEAN UP	0.3	0.0	0.3 HRS			38.8	1.60	1.61	06/04/96	02:30 PM	06/04/96	02:45 PM	
60	SUBTOTAL	25.0		25.0 HRS		38.5								
61														
62	2 B FLASK GROWTH													
63														
64	SET UP	1.0	0.0	1.0 HRS	37.5			1.52	1.56	06/04/96	12:30 PM	06/04/96	01:30 PM	
65	PREINCUBATION	1.0	0.0	1.0 HRS	38.5			1.56	1.60	06/04/96	01:30 PM	06/04/96	02:30 PM	
66	INCUBATION	23.0	0.0	23.0 HRS		61.5		1.60	2.56	06/04/96	02:30 PM	06/05/96	01:30 PM	
67	CLEAN UP	0.3	0.0	0.3 HRS			61.8	2.56	2.57	06/05/96	01:30 PM	06/05/96	01:45 PM	
67	SUBTOTAL	25.0		25.0 HRS		61.5								
68														
69	3 B SEED FERMENTATION													
70														
71	SET UP	1.0	0.0	1.0 HRS	60.5			2.48	2.52	06/05/96	11:30 AM	06/05/96	12:30 PM	
72	PREINCUBATION	1.0	0.0	1.0 HRS	61.5			2.52	2.56	06/05/96	12:30 PM	06/05/96	01:30 PM	
73	FERMENTATION	21.0	0.0	21.0 HRS		82.5		2.56	3.44	06/05/96	01:30 PM	06/06/96	10:30 AM	
74	HARVEST	0.5	0.0	0.5 HRS		83.0		3.44	3.46	06/06/96	10:30 AM	06/06/96	11:00 AM	50.0 L 1.7 LPM = 0.50 HRS
75	CIP	1.0	0.0	1.0 HRS			83.5	3.44	3.48	06/06/96	10:30 AM	06/06/96	11:30 AM	
76	SIP	1.0	0.0	1.0 HRS			84.5	3.48	3.52	06/06/96	11:30 AM	06/06/96	12:30 PM	
77	CLEAN UP	3.0	0.0	3.0 HRS			87.5	3.52	3.65	06/06/96	12:30 PM	06/06/96	03:30 PM	
78	SUBTOTAL	28.5		28.5 HRS		83.0								
79														
80	4 B PRODUCTION FERMENTATION													
81														
82	SET UP	1.0	0.0	1.0 HRS	82.0			3.38	3.42	06/06/96	09:00 AM	06/06/96	10:00 AM	
83	PREINCUBATION	1.0	0.0	1.0 HRS	83.0			3.42	3.46	06/06/96	10:00 AM	06/06/96	11:00 AM	
84	FERMENTATION	21.0	0.0	21.0 HRS		104.0		3.46	4.33	06/06/96	11:00 AM	06/07/96	08:00 AM	

Replacement Sheet
Sheet 15 of 167
Appl. No. : 09/100,088; Filed: June 19, 1998
Dkt No. : 1606.002000-4; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 12B-2

85	CIP	1.0	0.0	1.0 HRS			105.0	4.33	4.38	06/07/96	08:00 AM	06/07/96	09:00 AM		
86	SIP	1.0	0.0	1.0 HRS			106.0	4.38	4.42	06/07/96	09:00 AM	06/07/96	10:00 AM		
87	CLEAN UP	2.0	0.0	2.0 HRS			108.0	4.42	4.50	06/07/96	10:00 AM	06/07/96	12:00 PM		
88	SUBTOTAL	27.0		27.0 HRS		104.0									
89															
90	5 B HEAT EXCHANGE														
91															
92	SET UP	0.50	0.0	0.5 HRS	104.5			4.33	4.35	06/07/96	08:00 AM	06/07/96	08:30 AM		
93	TRANSFER	1.00	0.0	1.0 HRS		105.0		4.33	4.38	06/07/96	08:00 AM	06/07/96	09:00 AM	562.1 L@	9.4 LPM = 1.00 HRS
94	CIP	1.0	0.0	1.0 HRS			106.0	4.38	4.42	06/07/96	09:00 AM	06/07/96	10:00 AM		
95	SIP	1.0	0.0	1.0 HRS			107.0	4.42	4.46	06/07/96	10:00 AM	06/07/96	11:00 AM		
96	CLEAN UP	2.0	0.0	2.0 HRS			109.0	4.46	4.54	06/07/96	11:00 AM	06/07/96	01:00 PM		
97	SUBTOTAL	5.0		5.0 HRS		105.0									
98															
99	6 B CONT. CENT./SOLIDS														
100															
101	SET UP	1.00	0.0	1.0 HRS	105.0			4.33	4.38	06/07/96	08:00 AM	06/07/96	09:00 AM		
102	CENTRIFUGATION	1.00	0.0	1.0 HRS		106.0		4.38	4.42	06/07/96	09:00 AM	06/07/96	10:00 AM	562.1 L@	9.4 LPM = 1.00 HRS
103	WASH	0.10	0.0	0.1 HRS		106.1		4.42	4.42	06/07/96	10:00 AM	06/07/96	10:06 AM	1.0 L@	0.2 LPM = 0.10 HRS
104	CIP	0.25	0.0	0.3 HRS			106.4	4.42	4.43	06/07/96	10:06 AM	06/07/96	10:21 AM	20.0 L@	1.3 LPM = 0.25 HRS
105	SIP	1.00	0.0	1.0 HRS			107.4	4.43	4.47	06/07/96	10:21 AM	06/07/96	11:21 AM		
106	CLEAN UP	0.50	0.0	0.5 HRS			107.9	4.47	4.49	06/07/96	11:21 AM	06/07/96	11:51 AM		
107	SUBTOTAL	3.85		3.85 HRS		106.1									
108															
109	1 C INOCULUM PREP														
110															
111	SET UP	1.0	0.0	1.0 HRS	14.5			0.56	0.50	06/03/96	01:30 PM	06/03/96	02:30 PM		
112	PREINCUBATION	1.0	0.0	1.0 HRS	15.5			0.60	0.65	06/03/96	02:30 PM	06/03/96	03:30 PM		
113	INCUBATION	23.0	0.0	23.0 HRS		38.5		0.65	1.60	06/03/96	03:30 PM	06/04/96	02:30 PM		
114	CLEAN UP	0.3	0.0	0.3 HRS			38.8	1.60	1.61	06/04/96	02:30 PM	06/04/96	02:45 PM		
114	SUBTOTAL	25.0		25.0 HRS		38.5									
115															

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Appl. No. : 09/100,088; Filed: June 19, 1998
Dkt No. : 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 12C-1

	OPERATION	PROCESS TIME LINE DURATION (HRS.) CALC.	A/D	ADJ.	REL. TIME SCALE (HRS) PREP	EXEC.	CONPL.	ABS. DAYS START	END	START DATE	TIME	FINISH DATE	TIME	CALCULATIONS
						15.5				06/03/96	08:00 AM			
116	2 C FLASK GROWTH													
117														
118	SET UP	1.0	0.0	1.0 HRS	37.5			1.52	1.56	06/04/96	12:30 PM	06/04/96	01:30 PM	
119	PREINCUBATION	1.0	0.0	1.0 HRS	38.5			1.56	1.60	06/04/96	01:30 PM	06/04/96	02:30 PM	
120	INCUBATION	23.0	0.0	23.0 HRS		61.5		1.60	2.56	06/04/96	02:30 PM	06/05/96	01:30 PM	
121	CLEAN UP	0.3	0.0	0.3 HRS			61.8	2.56	2.57	06/05/96	01:30 PM	06/05/96	01:45 PM	
121	SUBTOTAL	25.0		25.0 HRS		61.5								
122														
123	3 C SEED FERMENTATION													
124														
125	SET UP	1.0	0.0	1.0 HRS	60.5			2.48	2.52	06/05/96	11:30 AM	06/05/96	12:30 PM	
126	PREINCUBATION	1.0	0.0	1.0 HRS	61.5			2.52	2.56	06/05/96	12:30 PM	06/05/96	01:30 PM	
127	FERMENTATION	21.0	0.0	21.0 HRS		82.5		2.56	3.44	06/05/96	01:30 PM	06/06/96	10:30 AM	
128	HARVEST	0.5	0.0	0.5 HRS		83.0		3.44	3.46	06/06/96	10:30 AM	06/06/96	11:00 AM	50.0 L 1.7 LPM = 0.50 HRS
129	CIP	1.0	0.0	1.0 HRS			83.5	3.44	3.48	06/06/96	10:30 AM	06/06/96	11:30 AM	
130	SIP	1.0	0.0	1.0 HRS			84.5	3.48	3.52	06/06/96	11:30 AM	06/06/96	12:30 PM	
131	CLEAN UP	3.0	0.0	3.0 HRS			87.5	3.52	3.65	06/06/96	12:30 PM	06/06/96	03:30 PM	
132	SUBTOTAL	28.5		28.5 HRS		83.0								
133														
134	4 C PRODUCTION FERMENTATION													
135														
136	SET UP	1.0	0.0	1.0 HRS	82.0			3.38	3.42	06/06/96	09:00 AM	06/06/96	10:00 AM	
137	PREINCUBATION	1.0	0.0	1.0 HRS	83.0			3.42	3.46	06/06/96	10:00 AM	06/06/96	11:00 AM	
138	FERMENTATION	21.0	0.0	21.0 HRS		104.0		3.46	4.33	06/06/96	11:00 AM	06/07/96	08:00 AM	
139	CIP	1.0	0.0	1.0 HRS			105.0	4.33	4.38	06/07/96	08:00 AM	06/07/96	09:00 AM	
140	SIP	1.0	0.0	1.0 HRS			106.0	4.38	4.42	06/07/96	09:00 AM	06/07/96	10:00 AM	
141	CLEAN UP	2.0	0.0	2.0 HRS			108.0	4.42	4.50	06/07/96	10:00 AM	06/07/96	12:00 PM	
142	SUBTOTAL	27.0		27.0 HRS		104.0								

Replacement Sheet
Sheet 17 of 167
Appl. No. : 09/100,088; Filed: June 19, 1998
Dkt No. : 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 12C-2

143															
144	5 C HEAT EXCHANGE														
145															
146	SET UP	0.50	0.0	0.5 HRS	104.5			4.33	4.35	06/07/96	08:00 AM	06/07/96	08:30 AM		
147	TRANSFER	1.00	0.0	1.0 HRS		105.0		4.33	4.38	06/07/96	08:00 AM	06/07/96	09:00 AM	562.1 LB	9.4 LPM = 1.00 HRS
148	CIP	1.0	0.0	1.0 HRS			106.0	4.38	4.42	06/07/96	09:00 AM	06/07/96	10:00 AM		
149	SIP	1.0	0.0	1.0 HRS			107.0	4.42	4.46	06/07/96	10:00 AM	06/07/96	11:00 AM		
150	CLEAN UP	2.0	0.0	2.0 HRS			109.0	4.46	4.54	06/07/96	11:00 AM	06/07/96	01:00 PM		
151	SUBTOTAL	5.0		5.0 HRS		105.0									
152															
153	6 C CONT. CENT./SOLIDS														
154															
155	SET UP	1.00	0.0	1.0 HRS	105.0			4.33	4.38	06/07/96	08:00 AM	06/07/96	09:00 AM		
156	CENTRIFUGATION	1.00	0.0	1.0 HRS		106.0		4.38	4.42	06/07/96	09:00 AM	06/07/96	10:00 AM	562.1 LB	9.4 LPM = 1.00 HRS
157	WASH	0.10	0.0	0.1 HRS		106.1		4.42	4.42	06/07/96	10:00 AM	06/07/96	10:06 AM	1.0 LB	0.2 LPM = 0.10 HRS
158	CIP	0.25	0.0	0.3 HRS			106.4	4.42	4.43	06/07/96	10:06 AM	06/07/96	10:21 AM	20.0 LB	1.3 LPM = 0.25 HRS
159	SIP	1.00	0.0	1.0 HRS			107.4	4.43	4.47	06/07/96	10:21 AM	06/07/96	11:21 AM		
160	CLEAN UP	0.50	0.0	0.5 HRS			107.9	4.47	4.49	06/07/96	11:21 AM	06/07/96	11:51 AM		
161	SUBTOTAL	3.85		3.85 HRS		106.1									
162															
163	7 A RESOLUBLIZATION														
164															
165	SET UP	1.00	0.0	1.0 HRS	106.1			4.38	4.42	06/07/96	09:06 AM	06/07/96	10:06 AM		
166	DILUTION	0.50	0.0	0.5 HRS		106.6		4.42	4.44	06/07/96	10:06 AM	06/07/96	10:36 AM	46.7 LB	1.6 LPM = 0.50 HRS
167	AGITATE	1.00	0.0	1.0 HRS		107.6		4.44	4.48	06/07/96	10:36 AM	06/07/96	11:36 AM		0.50 HRS
168	CIP	1.00	0.0	1.0 HRS			108.6	4.48	4.53	06/07/96	11:36 AM	06/07/96	12:36 PM		
169	SIP	1.00	0.0	1.0 HRS			109.6	4.53	4.57	06/07/96	12:36 PM	06/07/96	01:36 PM		
170	CLEAN UP	1.00	0.0	1.0 HRS			110.6	4.57	4.61	06/07/96	01:36 PM	06/07/96	02:36 PM		
171	SUBTOTAL	5.50		5.50 HRS		107.6									
172															
173	8 A HEAT EXCHANGE														
174															

FIG. 12D-1

	OPERATION	PROCESS TIME LINE												CALCULATIONS
		DURATION (HRS.)			REL. TIME SCALE (HRS)			ABS. DAYS		START		FINISH		
		CALC.	A/D	ADJ.	PREP	EXEC.	COMPL.	START	END	DATE	TIME	DATE	TIME	
						15.5				06/03/96	08:00 AM			
175	SET UP	0.50	0.0	0.5 HRS	107.6			4.46	4.48	06/07/96	11:06 AM	06/07/96	11:36 AM	
176	TRANSFER	0.30	0.0	0.3 HRS		107.9		4.48	4.50	06/07/96	11:36 AM	06/07/96	11:54 AM	66.5 L@ 3.7 LPM = 0.30 HRS
177	CIP	0.0	0.0	0.0 HRS			107.9	4.50	4.50	06/07/96	11:54 AM	06/07/96	11:54 AM	
178	SIP	0.0	0.0	0.0 HRS			107.9	4.50	4.50	06/07/96	11:54 AM	06/07/96	11:54 AM	
179	CLEAN UP	0.0	0.0	0.0 HRS			107.9	4.50	4.50	06/07/96	11:54 AM	06/07/96	11:54 AM	
180	SUBTOTAL	0.8		0.8 HRS		107.9								
181														
182	9 A HOMMOGENIZATION													
183														
184	SET UP	0.25	0.0	0.3 HRS	107.9			4.49	4.50	06/07/96	11:39 AM	06/07/96	11:54 AM	
185	LYSIS	0.68	0.0	0.7 HRS		108.6		4.50	4.52	06/07/96	11:54 AM	06/07/96	12:34 PM	66.5 L@ 1.6 LPM = 0.68 HRS
186	CIP	0.0	0.0	0.0 HRS			108.6	4.52	4.52	06/07/96	12:34 PM	06/07/96	12:34 PM	
187	SIP	0.0	0.0	0.0 HRS			108.6	4.52	4.52	06/07/96	12:34 PM	06/07/96	12:34 PM	
188	CLEAN UP	0.0	0.0	0.0 HRS			108.6	4.52	4.52	06/07/96	12:34 PM	06/07/96	12:34 PM	
189	SUBTOTAL	0.9		0.9 HRS		108.6								
190														
191	10 A HEAT EXCHANGE													
192														
193	SET UP	0.50	0.0	0.5 HRS	108.6			4.50	4.52	06/07/96	12:04 PM	06/07/96	12:34 PM	
194	TRANSFER	0.30	0.0	0.3 HRS		108.9		4.52	4.54	06/07/96	12:34 PM	06/07/96	12:52 PM	69.0 L@ 3.8 LPM = 0.30 HRS
195	CIP	0.0	0.0	0.0 HRS			108.9	4.54	4.54	06/07/96	12:52 PM	06/07/96	12:52 PM	
196	SIP	0.0	0.0	0.0 HRS			108.9	4.54	4.54	06/07/96	12:52 PM	06/07/96	12:52 PM	
197	CLEAN UP	0.0	0.0	0.0 HRS			108.9	4.54	4.54	06/07/96	12:52 PM	06/07/96	12:52 PM	
198	SUBTOTAL	0.8		0.8 HRS		108.9								
199														
200	8 B HEAT EXCHANGE													
201														
202	SET UP	0.00	0.0	0.0 HRS	108.9			4.54	4.54	06/07/96	12:52 PM	06/07/96	12:52 PM	

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Appl. No. : 09/100,088; Filed: June 19, 1998
Dkt No. : 1606.002000-4; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 12D-2

203	TRANSFER	0.30	0.0	0.3 HRS		109.2		4.54	4.55	06/07/96	12:52 PM	06/07/96	01:10 PM	66.5 LB	3.7 LPM = 0.30 HRS
204	CIP	0.0	0.0	0.0 HRS			109.2	4.55	4.55	06/07/96	01:10 PM	06/07/96	01:10 PM		
205	SIP	0.0	0.0	0.0 HRS			109.2	4.55	4.55	06/07/96	01:10 PM	06/07/96	01:10 PM		
206	CLEAN UP	0.0	0.0	0.0 HRS			109.2	4.55	4.55	06/07/96	01:10 PM	06/07/96	01:10 PM		
207	SUBTOTAL	0.3		0.3 HRS		109.2									
208															
209	9 B HOMMOGENIZATION														
210															
211	SET UP	0.00	0.0	0.0 HRS	109.2			4.55	4.55	06/07/96	01:10 PM	06/07/96	01:10 PM		
212	LYSIS	0.68	0.0	0.7 HRS		109.9		4.55	4.58	06/07/96	01:10 PM	06/07/96	01:51 PM	66.5 LB	1.6 LPM = 0.68 HRS
213	CIP	0.0	0.0	0.0 HRS			109.9	4.58	4.58	06/07/96	01:51 PM	06/07/96	01:51 PM		
214	SIP	0.0	0.0	0.0 HRS			109.9	4.58	4.58	06/07/96	01:51 PM	06/07/96	01:51 PM		
215	CLEAN UP	0.0	0.0	0.0 HRS			109.9	4.58	4.58	06/07/96	01:51 PM	06/07/96	01:51 PM		
216	SUBTOTAL	0.7		0.7 HRS		109.9									
217															
218	10 B HEAT EXCHANGE														
219															
220	SET UP	0.50	0.0	0.5 HRS	109.9			4.56	4.58	06/07/96	01:21 PM	06/07/96	01:51 PM		
221	TRANSFER	0.30	0.0	0.3 HRS		110.2		4.58	4.59	06/07/96	01:51 PM	06/07/96	02:09 PM	69.0 LB	3.8 LPM = 0.30 HRS
222	CIP	0.0	0.0	0.0 HRS			110.2	4.59	4.59	06/07/96	02:09 PM	06/07/96	02:09 PM		
223	SIP	0.0	0.0	0.0 HRS			110.2	4.59	4.59	06/07/96	02:09 PM	06/07/96	02:09 PM		
224	CLEAN UP	0.0	0.0	0.0 HRS			110.2	4.59	4.59	06/07/96	02:09 PM	06/07/96	02:09 PM		
225	SUBTOTAL	0.8		0.8 HRS		110.2									
226															
227	8 C HEAT EXCHANGE														
228															
229	SET UP	0.00	0.0	0.0 HRS	110.2			4.59	4.59	06/07/96	02:09 PM	06/07/96	02:09 PM		
230	TRANSFER	0.30	0.0	0.3 HRS		110.5		4.59	4.60	06/07/96	02:09 PM	06/07/96	02:27 PM	66.5 LB	3.7 LPM = 0.30 HRS
231	CIP	1.0	0.0	1.0 HRS			111.5	4.60	4.64	06/07/96	02:27 PM	06/07/96	03:27 PM		
232	SIP	1.0	0.0	1.0 HRS			112.5	4.64	4.69	06/07/96	03:27 PM	06/07/96	04:27 PM		
233	CLEAN UP	1.0	0.0	1.0 HRS			113.5	4.69	4.73	06/07/96	04:27 PM	06/07/96	05:27 PM		
234	SUBTOTAL	3.3		3.3 HRS		110.5									

Appl. No. : 09/100,088; Filed: June 19, 1998
Dkt No. : 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 12E-1

	OPERATION	PROCESS TIME LINE DURATION (HRS.) CALC.	A/D	ADJ.	REL. TIME SCALE (HRS) PREP	EXEC.	COMPL.	ABS. DAYS START	END	START DATE	START TIME	FINISH DATE	FINISH TIME	CALCULATIONS
235						15.5				06/03/96	08:00 AM			
236	9 C HOMOGENIZATION													
237														
238	SET UP	0.00	0.0	0.0 HRS	110.5			4.60	4.60	06/07/96	02:27 PM	06/07/96	02:27 PM	
239	LYSIS	0.68	0.0	0.7 HRS		111.1		4.60	4.63	06/07/96	02:27 PM	06/07/96	03:07 PM	66.5 LB 1.6 LPM = 0.68 HRS
240	CIP	1.0	0.0	1.0 HRS			112.1	4.63	4.67	06/07/96	03:07 PM	06/07/96	04:07 PM	
241	SIP	1.0	0.0	1.0 HRS			113.1	4.67	4.71	06/07/96	04:07 PM	06/07/96	05:07 PM	
242	CLEAN UP	1.0	0.0	1.0 HRS			114.1	4.71	4.76	06/07/96	05:07 PM	06/07/96	06:07 PM	
243	SUBTOTAL	3.7		3.7 HRS		111.1								
244														
245	10 C HEAT EXCHANGE													
246														
247	SET UP	0.00	0.0	0.0 HRS	111.1			4.63	4.63	06/07/96	03:07 PM	06/07/96	03:07 PM	
248	TRANSFER	0.30	0.0	0.3 HRS		111.4		4.63	4.64	06/07/96	03:07 PM	06/07/96	03:25 PM	69.0 LB 3.8 LPM = 0.30 HRS
249	CIP	1.0	0.0	1.0 HRS			112.4	4.64	4.68	06/07/96	03:25 PM	06/07/96	04:25 PM	
250	SIP	1.0	0.0	1.0 HRS			113.4	4.68	4.73	06/07/96	04:25 PM	06/07/96	05:25 PM	
251	CLEAN UP	1.0	0.0	1.0 HRS			114.4	4.73	4.77	06/07/96	05:25 PM	06/07/96	06:25 PM	
252	SUBTOTAL	3.3		3.3 HRS		111.4								
253														
254	11 A RESOLUBILIZATION													
255														
256	SET UP	1.0	0.0	1.0 HRS	108.9			4.49	4.54	06/07/96	11:52 AM	06/07/96	12:52 PM	
257	DILUTION	0.5	0.0	0.5 HRS		108.4		4.54	4.55	06/07/96	12:52 PM	06/07/96	01:22 PM	206.9 LB 6.9 LPM = 0.50 HRS
258	AGITATE	0.5	0.0	0.5 HRS		109.9		4.55	4.58	06/07/96	01:22 PM	06/07/96	01:52 PM	0.50 HRS
259	CIP	0.0	0.0	0.0 HRS			109.9	4.58	4.58	06/07/96	01:52 PM	06/07/96	01:52 PM	
260	SIP	0.0	0.0	0.0 HRS			109.9	4.58	4.58	06/07/96	01:52 PM	06/07/96	01:52 PM	
261	CLEAN UP	0.0	0.0	0.0 HRS			109.9	4.58	4.58	06/07/96	01:52 PM	06/07/96	01:52 PM	
262	SUBTOTAL	2.0		2.0 HRS		109.9								

FIG. 12E-2

263															
264	12 A CONT. CENT/SOLIDS														
265															
266	SET UP	1.0	0.0	1.0 HRS	109.9			4.54	4.58	06/07/96	12:52 PM	06/07/96	01:52 PM		
267	CENTRIFUGATION	0.5	0.0	0.5 HRS		110.4		4.58	4.60	06/07/96	01:52 PM	06/07/96	02:22 PM	275.9 L@	9.2 LPM = 0.50 HRS
268	WASH	0.1	0.0	0.1 HRS		110.5		4.60	4.60	06/07/96	02:22 PM	06/07/96	02:28 PM	3.0 L@	0.5 LPM = 0.10 HRS
269	CIP	0.0	0.0	0.0 HRS			110.5	4.60	4.60	06/07/96	02:28 PM	06/07/96	02:28 PM	8.0 L@	0.5 LPM = 0.25 HRS
270	SIP	0.0	0.0	0.0 HRS			110.5	4.60	4.60	06/07/96	02:28 PM	06/07/96	02:28 PM		
271	CLEAN UP	0.0	0.0	0.0 HRS			110.5	4.60	4.60	06/07/96	02:28 PM	06/07/96	02:28 PM		
272	SUBTOTAL	1.6		1.6 HRS		110.5									
273															
274	11 B RESOLUBLIZATION														
275															
276	SET UP	0.0	0.0	0.0 HRS	110.5			4.60	4.60	06/07/96	02:28 PM	06/07/96	02:28 PM		
277	DILUTION	0.5	0.0	0.5 HRS		111.0		4.60	4.62	06/07/96	02:28 PM	06/07/96	02:58 PM	206.9 L@	6.9 LPM = 0.50 HRS
278	AGITATE	0.3	0.0	0.3 HRS		111.2		4.62	4.63	06/07/96	02:58 PM	06/07/96	03:13 PM		0.50 HRS
279	CIP	1.0	0.0	1.0 HRS			112.2	4.63	4.68	06/07/96	03:13 PM	06/07/96	04:13 PM		
280	SIP	1.0	0.0	1.0 HRS			113.2	4.68	4.72	06/07/96	04:13 PM	06/07/96	05:13 PM		
281	CLEAN UP	1.0	0.0	1.0 HRS			114.2	4.72	4.76	06/07/96	05:13 PM	06/07/96	06:13 PM		
282	SUBTOTAL	3.8		3.8 HRS		111.2									
283															
284	12 B CONT. CENT/SOLIDS														
285															
286	SET UP	1.0	0.0	1.0 HRS	111.2			4.59	4.63	06/07/96	02:13 PM	06/07/96	03:13 PM		
287	CENTRIFUGATION	0.5	0.0	0.5 HRS		111.7		4.63	4.66	06/07/96	03:13 PM	06/07/96	03:43 PM	275.9 L@	9.2 LPM = 0.50 HRS
288	WASH	0.1	0.0	0.1 HRS		111.8		4.66	4.66	06/07/96	03:43 PM	06/07/96	03:49 PM	3.0 L@	0.5 LPM = 0.10 HRS
289	CIP	0.3	0.0	0.3 HRS			112.1	4.66	4.67	06/07/96	03:49 PM	06/07/96	04:04 PM	8.0 L@	0.5 LPM = 0.25 HRS
290	SIP	1.0	0.0	1.0 HRS			113.1	4.67	4.71	06/07/96	04:04 PM	06/07/96	05:04 PM		
291	CLEAN UP	0.5	0.0	0.5 HRS			113.6	4.71	4.73	06/07/96	05:04 PM	06/07/96	05:34 PM		
292	SUBTOTAL	3.4		3.4 HRS		111.8									
293															
294	13 A RESOLUBLIZATION														

FIG. 12F-1

	OPERATION	PROCESS TIME LINE												CALCULATIONS
		DURATION (HRS.)			REL. TIME SCALE (HRS)			ABS. DAYS		START		FINISH		
		CALC.	A/D	ADJ.	PREP	EXEC.	COMPL.	START	END	DATE	TIME	DATE	TIME	
						15.5				06/03/96	08:00 AM			
295														
296	SET UP	1.0	0.0	1.0 HRS	110.5			4.56	4.60	06/07/96	01:28 PM	06/07/96	02:28 PM	
297	DILUTION	0.5	0.0	0.5 HRS		111.0		4.60	4.62	06/07/96	02:28 PM	06/07/96	02:58 PM	60.7 L@ 2.0 LPM = 0.50 HRS
298	AGITATE	18.0	0.0	18.0 HRS		129.0		4.62	5.37	06/07/96	02:58 PM	06/08/96	08:58 AM	23.50 HRS
299	CIP	1.0	0.0	1.0 HRS			130.0	5.37	5.42	06/08/96	08:58 AM	06/08/96	09:58 AM	
300	SIP	1.0	0.0	1.0 HRS			131.0	5.42	5.46	06/08/96	09:58 AM	06/08/96	10:58 AM	
301	CLEAN UP	1.0	0.0	1.0 HRS			132.0	5.46	5.50	06/08/96	10:58 AM	06/08/96	11:58 AM	
302	SUBTOTAL	22.5		22.5 HRS		129.0								
303														
304	14 A CONCENTRATION													26.99 SF
305														
306	SET UP	1.0	0.0	1.0 HRS	127.6			5.28	5.32	06/08/96	06:38 AM	06/08/96	07:38 AM	
307	FLUSH	0.7	0.0	0.7 HRS	128.3			5.32	5.35	06/08/96	07:38 AM	06/08/96	08:18 AM	54.0 L@ 3.0 L/SF/Hr or 1.35 LPM
308	PRIME	0.7	0.0	0.7 HRS	129.0			5.35	5.37	06/08/96	08:18 AM	06/08/96	08:58 AM	54.0 L@ 3.0 L/SF/Hr or 1.35 LPM
309	CONCENTRATION	1.0	0.0	1.0 HRS		130.0		5.37	5.42	06/08/96	08:58 AM	06/08/96	09:58 AM	81.0 L@ 3.0 L/SF/Hr or 1.35 LPM
310	DILUTION	0.4	0.0	0.4 HRS		130.4		5.42	5.43	06/08/96	09:58 AM	06/08/96	10:25 AM	13.5 L@ 0.5 LPM
311	WASH	0.9	0.0	0.9 HRS		131.3		5.43	5.47	06/08/96	10:25 AM	06/08/96	11:19 AM	72.9 L@ 3.0 L/SF/Hr or 1.35 LPM
312	FLUSH	0.3	0.0	0.3 HRS			131.7	5.47	5.49	06/08/96	11:19 AM	06/08/96	11:39 AM	27.0 L@ 3.0 L/SF/Hr or 1.35 LPM
313	STORE	0.7	0.0	0.7 HRS			132.3	5.49	5.51	06/08/96	11:39 AM	06/08/96	12:19 PM	54.0 L@ 3.0 L/SF/Hr or 1.35 LPM
314	CIP	1.0	0.0	1.0 HRS			133.3	5.51	5.56	06/08/96	12:19 PM	06/08/96	01:19 PM	
315	SIP	1.0	0.0	1.0 HRS			134.3	5.56	5.60	06/08/96	01:19 PM	06/08/96	02:19 PM	
316	CLEAN UP	1.0	0.0	1.0 HRS			135.3	5.60	5.64	06/08/96	02:19 PM	06/08/96	03:19 PM	
317	SUBTOTAL	8.7		8.7 HRS		131.3								MAX FR 1.35 LPM
318														
319	15 A MICROFILTRATION													12.60 SF
320														
321	SET UP	1.0	0.0	1.0 HRS	131.1			5.42	5.46	06/08/96	10:03 AM	06/08/96	11:03 AM	
322	FLUSH	0.1	0.0	0.1 HRS	131.2			5.46	5.47	06/08/96	11:03 AM	06/08/96	11:11 AM	25.2 L@ 15.0 L/SF/Hr or 3.15 LPM
323	PRIME	0.1	0.0	0.1 HRS	131.3			5.47	5.47	06/08/96	11:11 AM	06/08/96	11:19 AM	25.2 L@ 15.0 L/SF/Hr or 3.15 LPM

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Appl. No. : 09/100,088; Filed: June 19, 1998
Dkt No. : 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 12F-2

324	FILTRATION	0.5	0.0	0.5 HRS		131.8		5.47	5.49	06/08/96	11:19 AM	06/08/96	11:49 AM	94.5 LØ	15.0 L/SF/Hr or 3.15 LPM
325	WASH	0.0	0.0	0.0 HRS		131.8		5.49	5.49	06/08/96	11:49 AM	06/08/96	11:49 AM	0.0 LØ	15.0 L/SF/Hr or 3.15 LPM
326	REGENERATE	0.0	0.0	0.0 HRS			131.9	5.49	5.49	06/08/96	11:49 AM	06/08/96	11:51 AM	6.3 LØ	15.0 L/SF/Hr or 3.15 LPM
327	STORE	0.1	0.0	0.1 HRS			131.9	5.49	5.50	06/08/96	11:51 AM	06/08/96	11:55 AM	12.6 LØ	15.0 L/SF/Hr or 3.15 LPM
328	CIP	1.0	0.0	1.0 HRS			132.9	5.50	5.54	06/08/96	11:55 AM	06/08/96	12:55 PM		
329	SIP	1.0	0.0	1.0 HRS			133.9	5.54	5.58	06/08/96	12:55 PM	06/08/96	01:55 PM		
330	CLEAN UP	1.0	0.0	1.0 HRS			134.9	5.58	5.62	06/08/96	01:55 PM	06/08/96	02:55 PM		
331	SUBTOTAL	4.9		4.9 HRS		131.8									
332															
333	16 A P/A MPLC													63.8 L.CV	0.4 H/D 60.32 CM DIA.
334															
335	EQUILIBRATION	1.1	0.0	1.1 HRS	131.4			5.43	5.48	06/08/96	10:17 AM	06/08/96	11:24 AM	318.9 LØ	100.0 CM/HR or 4.76 LPM
336	LOAD	0.7	0.0	0.7 HRS		132.5		5.49	5.52	06/08/96	11:49 AM	06/08/96	12:31 PM	100.5 LØ	50.0 CM/HR or 2.38 LPM
337	WASH	1.3	0.0	1.3 HRS		133.9		5.52	5.58	06/08/96	12:31 PM	06/08/96	01:52 PM	191.4 LØ	50.0 CM/HR or 2.38 LPM
338	ELUTE A	1.3	0.0	1.3 HRS		135.2		5.58	5.63	06/08/96	01:52 PM	06/08/96	03:12 PM	191.4 LØ	50.0 CM/HR or 2.38 LPM
339	ELUTE B	0.0	0.0	0.0 HRS		135.2		5.63	5.63	06/08/96	03:12 PM	06/08/96	03:12 PM	0.0 LØ	30.0 CM/HR or 1.43 LPM
340	REGENERATE	0.2	0.0	0.2 HRS			135.4	5.63	5.64	06/08/96	03:12 PM	06/08/96	03:25 PM	63.8 LØ	100.0 CM/HR or 4.76 LPM
341	STORE	0.4	0.0	0.4 HRS			135.9	5.64	5.66	06/08/96	03:25 PM	06/08/96	03:52 PM	127.6 LØ	100.0 CM/HR or 4.76 LPM
342	CIP	1.0	0.0	1.0 HRS			136.9	5.66	5.70	06/08/96	03:52 PM	06/08/96	04:52 PM		
343	SIP	1.0	0.0	1.0 HRS			137.9	5.70	5.74	06/08/96	04:52 PM	06/08/96	05:52 PM		
344	CLEAN UP	1.0	0.0	1.0 HRS			138.9	5.74	5.79	06/08/96	05:52 PM	06/08/96	06:52 PM		
345	SUBTOTAL	5.2		5.2 HRS		135.2									MAX FR 4.76 LPM
346															
347															
348	17 A P/A MPLC													12.2 L.CV	0.4 H/D 34.75 CM DIA.
349															
350	EQUILIBRATION	0.6	0.0	0.6 HRS	135.6			5.62	5.65	06/08/96	02:59 PM	06/08/96	03:38 PM	61.0 LØ	100.0 CM/HR or 1.58 LPM
351	LOAD	1.1	0.0	1.1 HRS		136.3		5.63	5.68	06/08/96	03:12 PM	06/08/96	04:17 PM	51.0 LØ	50.0 CM/HR or 0.79 LPM
352	WASH	0.8	0.0	0.8 HRS		137.1		5.68	5.71	06/08/96	04:17 PM	06/08/96	05:03 PM	36.6 LØ	50.0 CM/HR or 0.79 LPM
353	ELUTE A	0.8	0.0	0.8 HRS		137.8		5.71	5.74	06/08/96	05:03 PM	06/08/96	05:49 PM	36.6 LØ	50.0 CM/HR or 0.79 LPM
354	ELUTE B	0.0	0.0	0.0 HRS		137.8		5.74	5.74	06/08/96	05:49 PM	06/08/96	05:49 PM	0.0 LØ	30.0 CM/HR or 0.47 LPM

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Dkt No. : 1606.0020004; Group Unit: 2128
Invenior: Peter G. BROWN; Tel. No.: 202-371-2600
For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 12G-1

	OPERATION	PROCESS TIME LINE												CALCULATIONS
		DURATION (HRS.)			REL. TIME SCALE (HRS)			ABS. DAYS		START		FINISH		
		CALC.	A/D	ADJ.	PREP	EXEC.	COMPL.	START	END	DATE	TIME	DATE	TIME	
						15.5				06/03/96	08:00 AM			
355	REGENERATE	0.1	0.0	0.1 HRS			138.0	5.74	5.75	06/08/96	05:49 PM	06/08/96	05:57 PM	12.2 LB 100.0 CM/HR or 1.58 LPM
356	STORE	0.3	0.0	0.3 HRS			138.2	5.75	5.76	06/08/96	05:57 PM	06/08/96	06:13 PM	24.4 LB 100.0 CM/HR or 1.58 LPM
357	CIP	1.0	0.0	1.0 HRS			139.2	5.76	5.80	06/08/96	06:13 PM	06/08/96	07:13 PM	
358	SIP	1.0	0.0	1.0 HRS			140.2	5.80	5.84	06/08/96	07:13 PM	06/08/96	08:13 PM	
359	CLEAN UP	1.0	0.0	1.0 HRS			141.2	5.84	5.88	06/08/96	08:13 PM	06/08/96	09:13 PM	
360	SUBTOTAL	6.7		6.7 HRS		137.8								MAX FR 1.58 LPM
361														
362	18 A FLOW DIALYSIS													12.20 SF
363														
364	SET UP	1.0	0.0	1.0 HRS	136.5			5.65	5.69	06/08/96	03:29 PM	06/08/96	04:29 PM	
365	FLUSH	0.7	0.0	0.7 HRS	137.2			5.69	5.72	06/08/96	04:29 PM	06/08/96	05:09 PM	24.4 LB 3.0 L/SF/Hr or 0.61 LPM
366	PRIME	0.7	0.0	0.7 HRS	137.8			5.72	5.74	06/08/96	05:09 PM	06/08/96	05:49 PM	24.4 LB 3.0 L/SF/Hr or 0.61 LPM
367	DIALYSIS	1.0	0.0	1.0 HRS		138.8		5.74	5.78	06/08/96	05:49 PM	06/08/96	06:49 PM	36.6 LB 3.0 L/SF/Hr or 0.61 LPM
368	WASH	0.0	0.0	0.0 HRS		138.8		5.78	5.78	06/08/96	06:49 PM	06/08/96	06:49 PM	0.0 LB 3.0 L/SF/Hr or 0.61 LPM
369	FLUSH	0.3	0.0	0.3 HRS			139.2	5.78	5.80	06/08/96	06:49 PM	06/08/96	07:09 PM	12.2 LB 3.0 L/SF/Hr or 0.61 LPM
370	STORE	0.7	0.0	0.7 HRS			139.8	5.80	5.83	06/08/96	07:09 PM	06/08/96	07:49 PM	24.4 LB 3.0 L/SF/Hr or 0.61 LPM
371	CIP	1.0	0.0	1.0 HRS			140.8	5.83	5.87	06/08/96	07:49 PM	06/08/96	08:49 PM	
372	SIP	1.0	0.0	1.0 HRS			141.8	5.87	5.91	06/08/96	08:49 PM	06/08/96	09:49 PM	
373	CLEAN UP	1.0	0.0	1.0 HRS			142.8	5.91	5.95	06/08/96	09:49 PM	06/08/96	10:49 PM	
374	SUBTOTAL	7.3		7.3 HRS		138.8								MAX FR 0.61 LPM
375														
376	19 A P/A HPLC													7.0 L.CV 0.4 H/D 28.81 CM DIA.
377														
378	EQUILIBRATION	0.5	0.0	0.5 HRS	138.5			5.75	5.77	06/08/96	05:59 PM	06/08/96	06:31 PM	34.8 LB 100.0 CM/HR or 1.09 LPM
379	LOAD	0.2	0.0	0.2 HRS		139.1		5.78	5.79	06/08/96	06:49 PM	06/08/96	07:03 PM	7.3 LB 50.0 CM/HR or 0.54 LPM
380	WASH	0.6	0.0	0.6 HRS		139.7		5.79	5.82	06/08/96	07:03 PM	06/08/96	07:41 PM	20.9 LB 50.0 CM/HR or 0.54 LPM
381	ELUTE A	0.6	0.0	0.6 HRS		140.3		5.82	5.85	06/08/96	07:41 PM	06/08/96	08:20 PM	20.9 LB 50.0 CM/HR or 0.54 LPM
382	ELUTE B	0.0	0.0	0.0 HRS		140.3		5.85	5.85	06/08/96	08:20 PM	06/08/96	08:20 PM	0.0 LB 30.0 CM/HR or 0.33 LPM
383	REGENERATE	0.1	0.0	0.1 HRS			140.4	5.85	5.85	06/08/96	08:20 PM	06/08/96	08:26 PM	7.0 LB 100.0 CM/HR or 1.09 LPM

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Appl. No. : 09/100,088; Filed: June 19, 1998
Dkt No. : 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 12G-2

384	STORE	0.2	0.0	0.2 HRS			140.7	5.85	5.86	06/08/96	08:26 PM	06/08/96	08:39 PM	13.9 LB	100.0 CM/HR or 1.09 LPM
385	CIP	1.0	0.0	1.0 HRS			141.7	5.86	5.90	06/08/96	08:39 PM	06/08/96	09:39 PM		
386	SIP	1.0	0.0	1.0 HRS			142.7	5.90	5.94	06/08/96	09:39 PM	06/08/96	10:39 PM		
387	CLEAN UP	1.0	0.0	1.0 HRS			143.7	5.94	5.99	06/08/96	10:39 PM	06/08/96	11:39 PM		
388	SUBTOTAL	5.4		5.4 HRS		140.3									MAX FR 1.09 LPM
389															
390	20 A FLOW DIALYSIS														2.43 SF
391															
392	SET UP	0.0	0.0	0.0 HRS	139.0			5.79	5.79	06/08/96	07:00 PM	06/08/96	07:00 PM		
393	FLUSH	0.7	0.0	0.7 HRS	139.7			5.79	5.82	06/08/96	07:00 PM	06/08/96	07:40 PM	4.9 LB	3.0 L/SF/HR or 0.12 LPM
394	PRIME	0.7	0.0	0.7 HRS	140.3			5.82	5.85	06/08/96	07:40 PM	06/08/96	08:20 PM	4.9 LB	3.0 L/SF/HR or 0.12 LPM
395	DIALYSIS	2.0	0.0	2.0 HRS		142.3		5.85	5.93	06/08/96	08:20 PM	06/08/96	10:20 PM	14.6 LB	3.0 L/SF/HR or 0.12 LPM
396	WASH	0.0	0.0	0.0 HRS		142.3		5.93	5.93	06/08/96	10:20 PM	06/08/96	10:20 PM	0.0 LB	3.0 L/SF/HR or 0.12 LPM
397	FLUSH	0.3	0.0	0.3 HRS			142.7	5.93	5.94	06/08/96	10:20 PM	06/08/96	10:40 PM	2.4 LB	3.0 L/SF/HR or 0.12 LPM
398	STORE	0.7	0.0	0.7 HRS			143.3	5.94	5.97	06/08/96	10:40 PM	06/08/96	11:20 PM	4.9 LB	3.0 L/SF/HR or 0.12 LPM
399	CIP	0.0	0.0	0.0 HRS			143.3	5.97	5.97	06/08/96	11:20 PM	06/08/96	11:20 PM		
400	SIP	0.0	0.0	0.0 HRS			143.3	5.97	5.97	06/08/96	11:20 PM	06/08/96	11:20 PM		
401	CLEAN UP	0.0	1.0	1.0 HRS			144.3	5.97	6.01	06/08/96	11:20 PM	06/08/96	12:20 AM		
402	SUBTOTAL	4.3		5.3 HRS		142.3									MAX FR 0.12 LPM
403															
404	17 A P/A HPLC													5.3 L.CV	0.4 H/D 26.35 CM DIA.
405															
406	EQUILIBRATION	0.5	0.0	0.5 HRS	142.0			5.89	5.91	06/08/96	09:28 PM	06/08/96	09:57 PM	26.6 LB	100.0 CM/HR or 0.91 LPM
407	LOAD	0.1	0.0	0.1 HRS		142.4		5.93	5.94	06/08/96	10:20 PM	06/08/96	10:26 PM	2.9 LB	50.0 CM/HR or 0.45 LPM
408	WASH	0.6	0.0	0.6 HRS		143.0		5.94	5.96	06/08/96	10:26 PM	06/08/96	11:01 PM	16.0 LB	50.0 CM/HR or 0.45 LPM
409	ELUTE A	0.6	0.0	0.6 HRS		143.6		5.96	5.96	06/08/96	11:01 PM	06/08/96	11:36 PM	16.0 LB	50.0 CM/HR or 0.45 LPM
410	ELUTE B	0.0	0.0	0.0 HRS		143.6		5.96	5.98	06/08/96	11:36 PM	06/08/96	11:36 PM	0.0 LB	30.0 CM/HR or 0.27 LPM
411	REGENERATE	0.1	0.0	0.1 HRS			143.7	5.98	5.99	06/08/96	11:36 PM	06/08/96	11:42 PM	5.3 LB	100.0 CM/HR or 0.91 LPM
412	STORE	0.2	0.0	0.2 HRS			143.9	5.99	6.00	06/08/96	11:42 PM	06/08/96	11:54 PM	10.6 LB	100.0 CM/HR or 0.91 LPM
413	CIP	0.0	0.0	0.0 HRS			143.9	6.00	6.00	06/08/96	11:54 PM	06/08/96	11:54 PM		
414	SIP	0.0	0.0	0.0 HRS			143.9	6.00	6.00	06/08/96	11:54 PM	06/08/96	11:54 PM		

Replacement Sheet
Sheet 26 of 167
Appl. No. : 09/100,088; Filed: June 19, 1998
Dkt No. : 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 12H

	OPERATION	PROCESS TIME LINE												CALCULATIONS
		DURATION (HRS.)			REL. TIME SCALE (HRS)			ABS. DAYS		START		FINISH		
		CALC.	A/D	ADJ.	PREP	EXEC.	COMPL.	START	END	DATE	TIME	DATE	TIME	
						15.5				06/03/96	08:00 AM			
415	CLEAN UP	1.0	0.0	1.0 HRS			144.9	6.00	6.04	06/08/96	11:54 PM	06/09/96	12:54 AM	
416	SUBTOTAL	2.1		2.1 HRS		143.6								MAX FR 0.91 LPM
417														
418	22 A STERILE FILTRATION													0.09 SF
419														
420	SET UP	0.5	0.0	0.5 HRS	152.6			6.34	6.36	06/09/96	08:06 AM	06/09/96	06:36 AM	
421	FILTRATION	0.5	0.0	0.5 HRS		144.1		5.98	6.00	06/08/96	11:36 PM	06/09/96	12:06 AM	2.2 L@ 50.0 L/SF/Hr or 0.07 LPM
422	STORAGE	0.5	0.0	0.5 HRS			144.6	6.00	6.03	06/09/96	12:06 AM	06/09/96	12:36 AM	
423	CIP	0.0	0.0	0.0 HRS			144.6	6.03	6.03	06/09/96	12:36 AM	06/09/96	12:36 AM	
424	SIP	0.0	0.0	0.0 HRS			144.6	6.03	6.03	06/09/96	12:36 AM	06/09/96	12:36 AM	
425	CLEAN UP	1.0	0.0	1.0 HRS			145.6	6.03	6.07	06/09/96	12:36 AM	06/09/96	01:36 AM	
426	SUBTOTAL	1.5		1.5 HRS		144.1								MAX FR 0.07 LPM

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Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 13

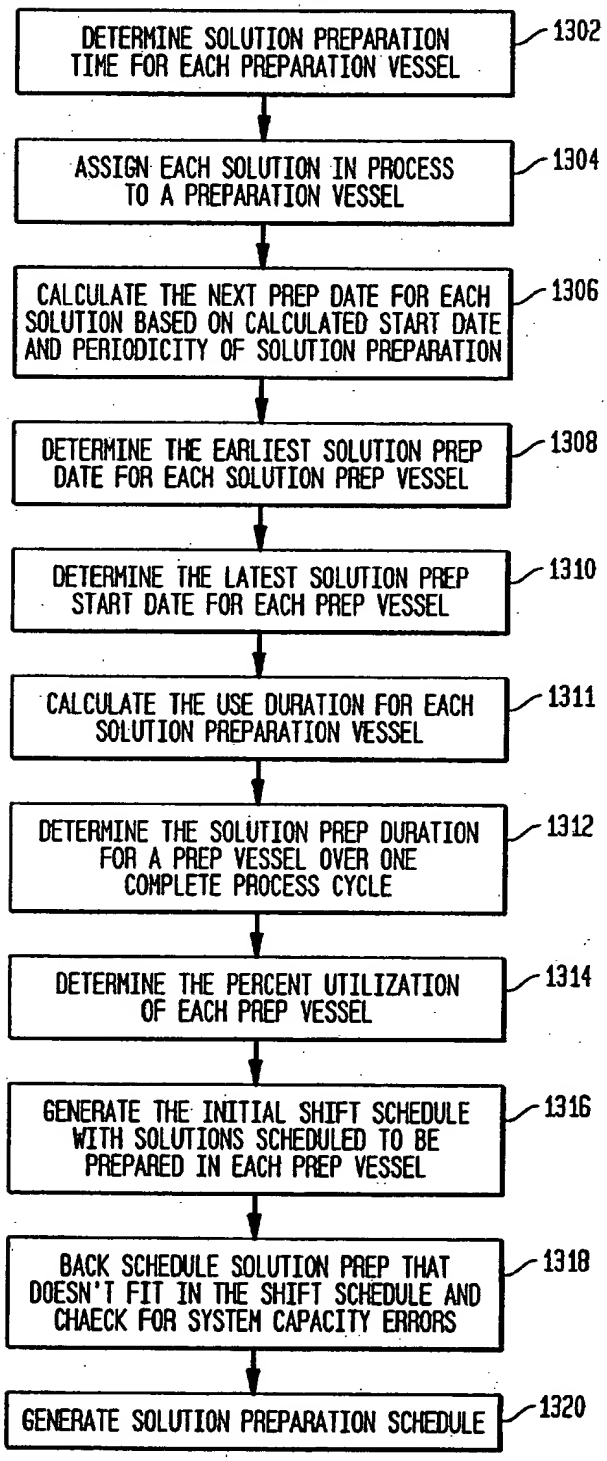


FIG. 14

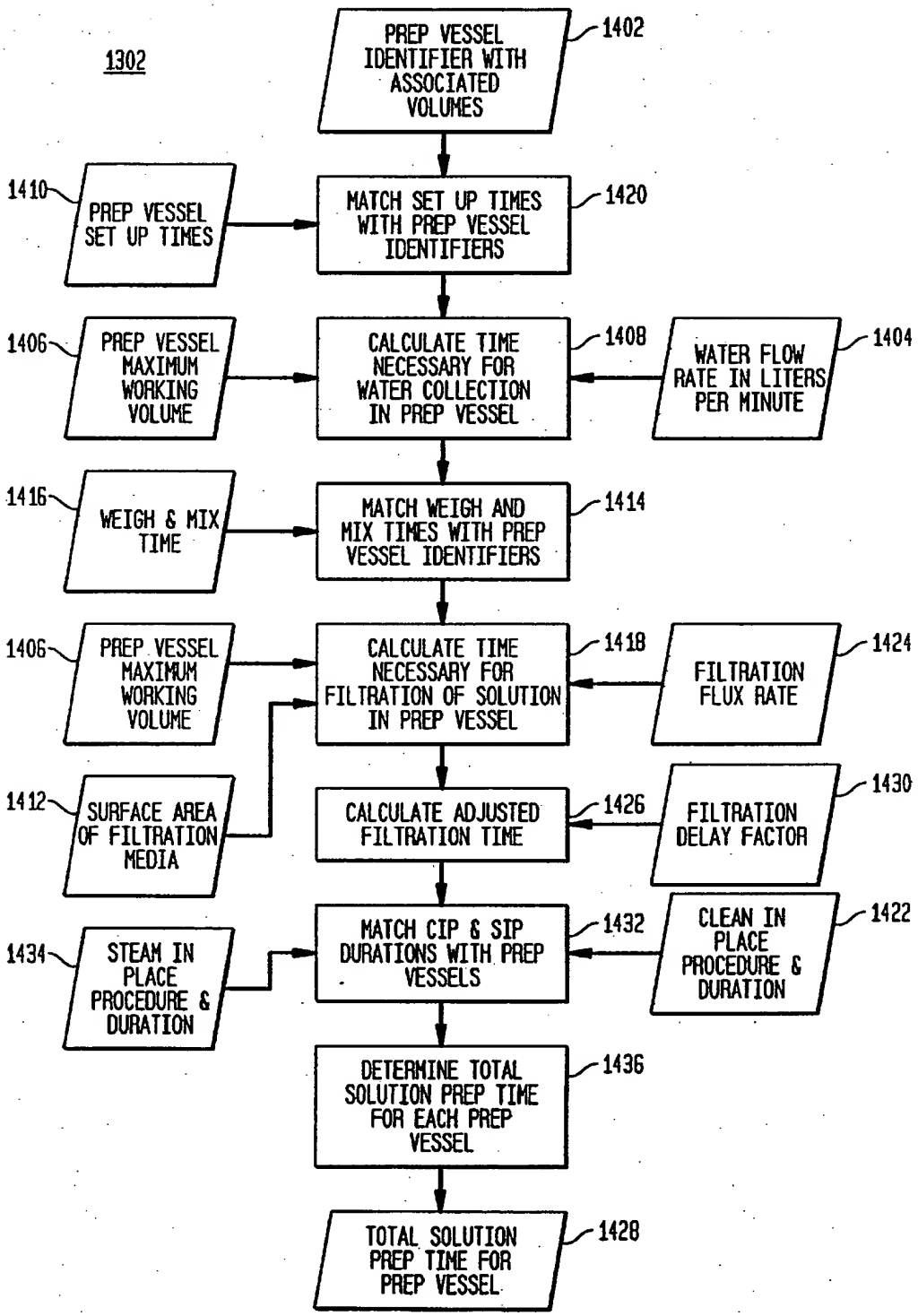
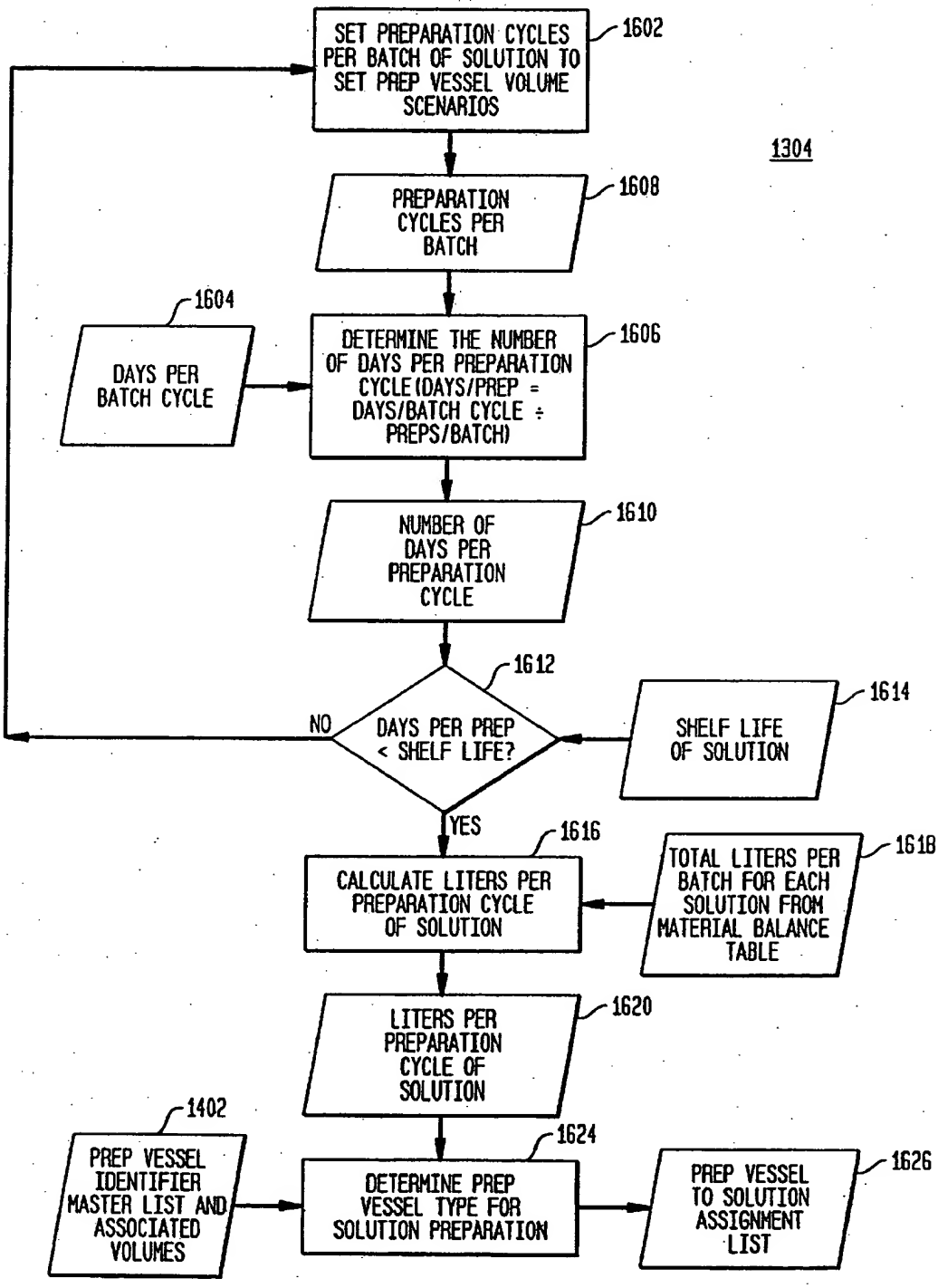

1302
PREP VESSEL IDENTIFIER WITH ASSOCIATED VOLUMES
1402
1410
PREP VESSEL SET UP TIMES
MATCH SET UP TIMES WITH PREP VESSEL IDENTIFIERS
1420
1406
PREP VESSEL MAXIMUM WORKING VOLUME
CALCULATE TIME NECESSARY FOR WATER COLLECTION IN PREP VESSEL
1408
WATER FLOW RATE IN LITERS PER MINUTE
1404
1416
WEIGH & MIX TIME
MATCH WEIGH AND MIX TIMES WITH PREP VESSEL IDENTIFIERS
1414
1406
PREP VESSEL MAXIMUM WORKING VOLUME
CALCULATE TIME NECESSARY FOR FILTRATION OF SOLUTION IN PREP VESSEL
1418
FILTRATION FLUX RATE
1424
1412
SURFACE AREA OF FILTRATION MEDIA
CALCULATE ADJUSTED FILTRATION TIME
1426
FILTRATION DELAY FACTOR
1430
1434
STEAM IN PLACE PROCEDURE & DURATION
MATCH CIP & SIP DURATIONS WITH PREP VESSELS
1432
CLEAN IN PLACE PROCEDURE & DURATION
1422
DETERMINE TOTAL SOLUTION PREP TIME FOR EACH PREP VESSEL
1436
TOTAL SOLUTION PREP TIME FOR PREP VESSEL
1428

FIG. 15

SOLUTION PREP VESSEL LIST/PROCEDURE

BATCH TANK		BATCH TANK			SET UP	WATER COLLECT.		WEIGH/	ULTRAFILTRATION/MICROFILTRATION					CIP			TOTAL		
NO.	MIN. LWV	NO.	MIN. LWV	MAX. LWV	MIN.	LPM.	MIN.	MIX MIN.	SF	L/SF/HR	MIN.	DELAY FACTOR	ADJ. MIN.	CYCLE	MIN.	SIP	MIN.	HRS.	PERC. UTIL.
101	0.5	101	0.5	1	10		1	15	0.5	25	4.8	1.2	5.76				31.76	0.5	
102	1	102	1	2	10		1	15	1	25	4.8	1.2	5.76				31.76	0.5	2%
103	2	103	2	4	20		2	30	1	25	9.6	1.2	11.52				63.52	1.1	
104	4	104	4	10	20	10	1	30	2	25	12	1.2	14.4				65.4	1.1	4%
105	10	105	10	20	20	10	2	30	2	25	24	1.2	28.8				80.8	1.3	
106	20	106	20	50	20	10	5	30	10	25	12	1.2	14.4	CIP-1	60	40	109.4	1.8	3%
107	50	107	50	100	20	10	10	30	10	25	24	1.2	28.8	CIP-1	60	40	128.8	2.1	8%
108	100	108	100	250	0.5	50	5	30	30	25	20	1.2	24	CIP-1	60	40	99.5	1.7	18%
109	250	109	250	500	0.5	50	10	30	30	25	40	1.2	48	CIP-1	60	40	128.5	2.1	11%
110	500	110	500	1,500	1	50	30	30	60	25	60	1.2	72	CIP-1	60	40	173	2.9	10%
111	1500	111	1500	3,000	1	50	60	30	60	25	120	1.2	144	CIP-1	60	40	275	4.6	16%
			1402	1406	1410	1404	1502	1410	1412	1424	1506				1422	1434	1428		

FIG. 16


SET PREPARATION CYCLES PER BATCH OF SOLUTION TO SET PREP VESSEL VOLUME SCENARIOS
1602
1304
PREPARATION CYCLES PER BATCH
1608
1604
DAYS PER BATCH CYCLE
DETERMINE THE NUMBER OF DAYS PER PREPARATION CYCLE (DAYS/PREP = DAYS/BATCH CYCLE ÷ PREPS/BATCH)
1606
NUMBER OF DAYS PER PREPARATION CYCLE
1610
1612
NO
DAYS PER PREP < SHELF LIFE?
SHELF LIFE OF SOLUTION
1614
YES
1616
CALCULATE LITERS PER PREPARATION CYCLE OF SOLUTION
TOTAL LITERS PER BATCH FOR EACH SOLUTION FROM MATERIAL BALANCE TABLE
1618
LITERS PER PREPARATION CYCLE OF SOLUTION
1620
1402
PREP VESSEL IDENTIFIER MASTER LIST AND ASSOCIATED VOLUMES
1624
DETERMINE PREP VESSEL TYPE FOR SOLUTION PREPARATION
PREP VESSEL TO SOLUTION ASSIGNMENT LIST
1626

Appl. No. : 09/100,088; Filed: June 19, 1998
Dkt No. : 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 17

Solution Prep Campaign Format

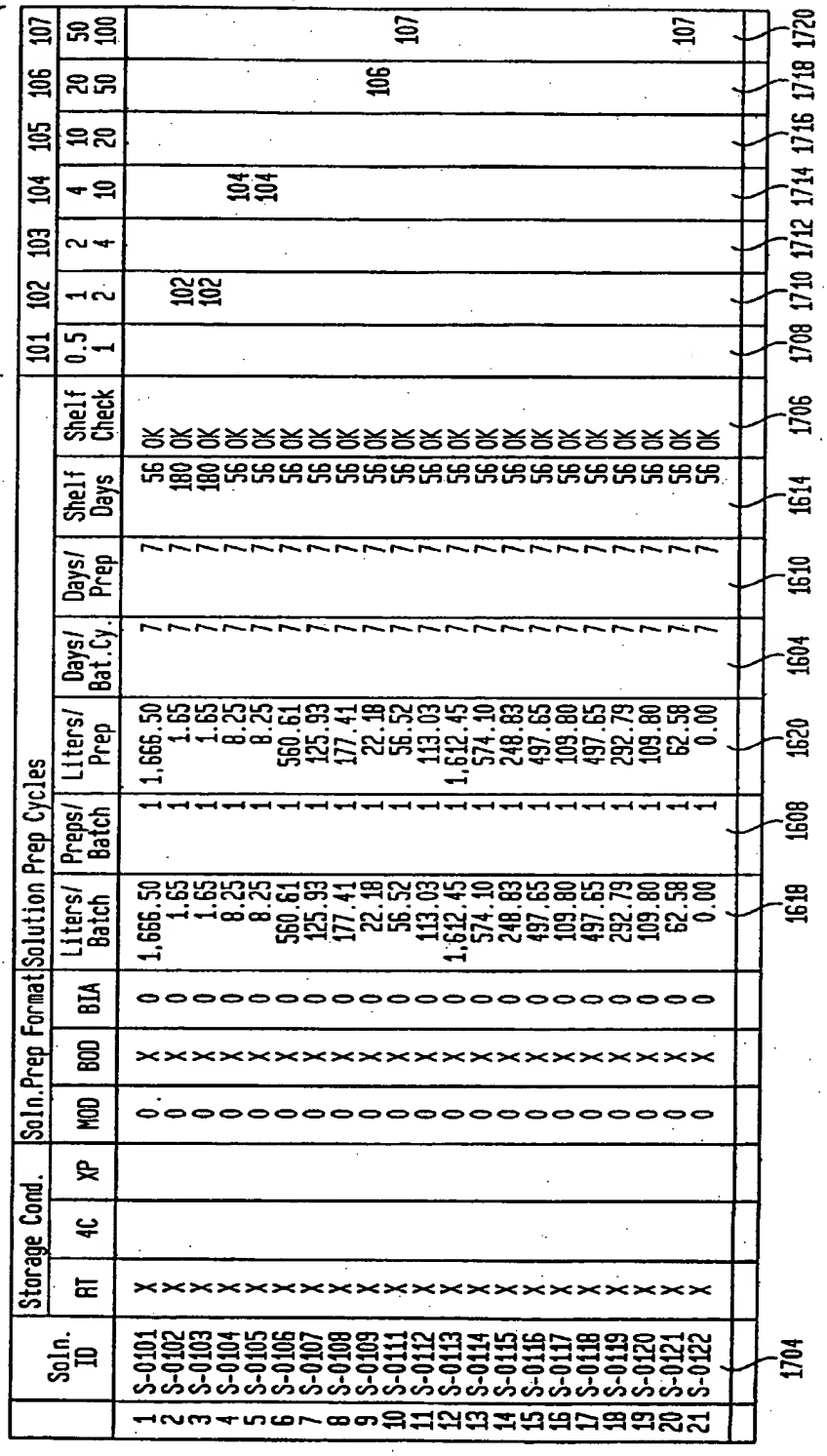


FIG. 18

Solution Prep Campaign Format

1626

	Soln. ID	108	109	110	111	Tank Assignment		Solution Prep Schedule								Tank Fill
		100 250	250 500	500 1500	1500 3000	Initial Assign.	Final Assign.	Required By	Back Days	Avail. By	Hold Days	Init. Start	Float Days	Final Start	Next Prep	Prep. Hrs.	101
1	S-0101				111	111	111	06/03/96	1	05/31/96	2	05/29/96	0	05/29/96	06/05/96	4	
2	S-0102					102	102	06/05/96	1	06/04/96	2	05/31/96	0	05/31/96	06/07/96	4	
3	S-0103					102	102	06/05/96	1	06/04/96	2	05/31/96	0	05/31/96	06/07/96	4	
4	S-0104					104	104	06/05/96	1	06/04/96	2	05/31/96	0	05/31/96	06/07/96	4	
5	S-0105					104	104	06/05/96	1	06/04/96	2	05/31/96	0	05/31/96	06/07/96	4	
6	S-0106			110		110	110	06/07/96	1	06/06/96	2	06/04/96	0	06/04/96	06/11/96	4	
7	S-0107	108				108	108	06/11/96	1	06/10/96	2	06/07/96	0	06/07/96	06/14/96	4	
8	S-0108	108				108	108	06/11/96	1	06/10/96	2	06/07/96	0	06/07/96	06/14/96	4	
9	S-0109					106	106	06/12/96	1	06/11/96	2	06/07/96	0	06/07/96	06/14/96	4	
10	S-0111					107	107	06/12/96	1	06/11/96	2	06/07/96	0	06/07/96	06/14/96	4	
11	S-0112	108				108	108	06/12/96	1	06/11/96	2	06/07/96	0	06/07/96	06/14/96	4	
12	S-0113				111	111	111	06/12/96	1	06/11/96	2	06/07/96	0	06/07/96	06/14/96	4	
13	S-0114			110		110	110	06/12/96	1	06/11/96	2	06/07/96	0	06/07/96	06/14/96	4	
14	S-0115	108				108	108	06/12/96	1	06/11/96	2	06/07/96	0	06/07/96	06/14/96	4	
15	S-0116		109			109	109	06/12/96	1	06/11/96	2	06/07/96	0	06/07/96	06/14/96	4	
16	S-0117	108				108	108	06/12/96	1	06/11/96	2	06/07/96	0	06/07/96	06/14/96	4	
17	S-0118		109			109	109	06/12/96	1	06/11/96	2	06/07/96	0	06/07/96	06/14/96	4	
18	S-0119		109			109	109	06/12/96	1	06/11/96	2	06/07/96	0	06/07/96	06/14/96	4	
19	S-0120	108				108	108	06/12/96	1	06/11/96	2	06/07/96	0	06/07/96	06/14/96	4	
20	S-0121					107	107	06/12/96	1	06/11/96	2	06/07/96	0	06/07/96	06/14/96	4	
21	S-0122					0	0	06/12/96	1	06/11/96	2	06/07/96	0	06/07/96	06/14/96	4	

1722 1724 1726 1728

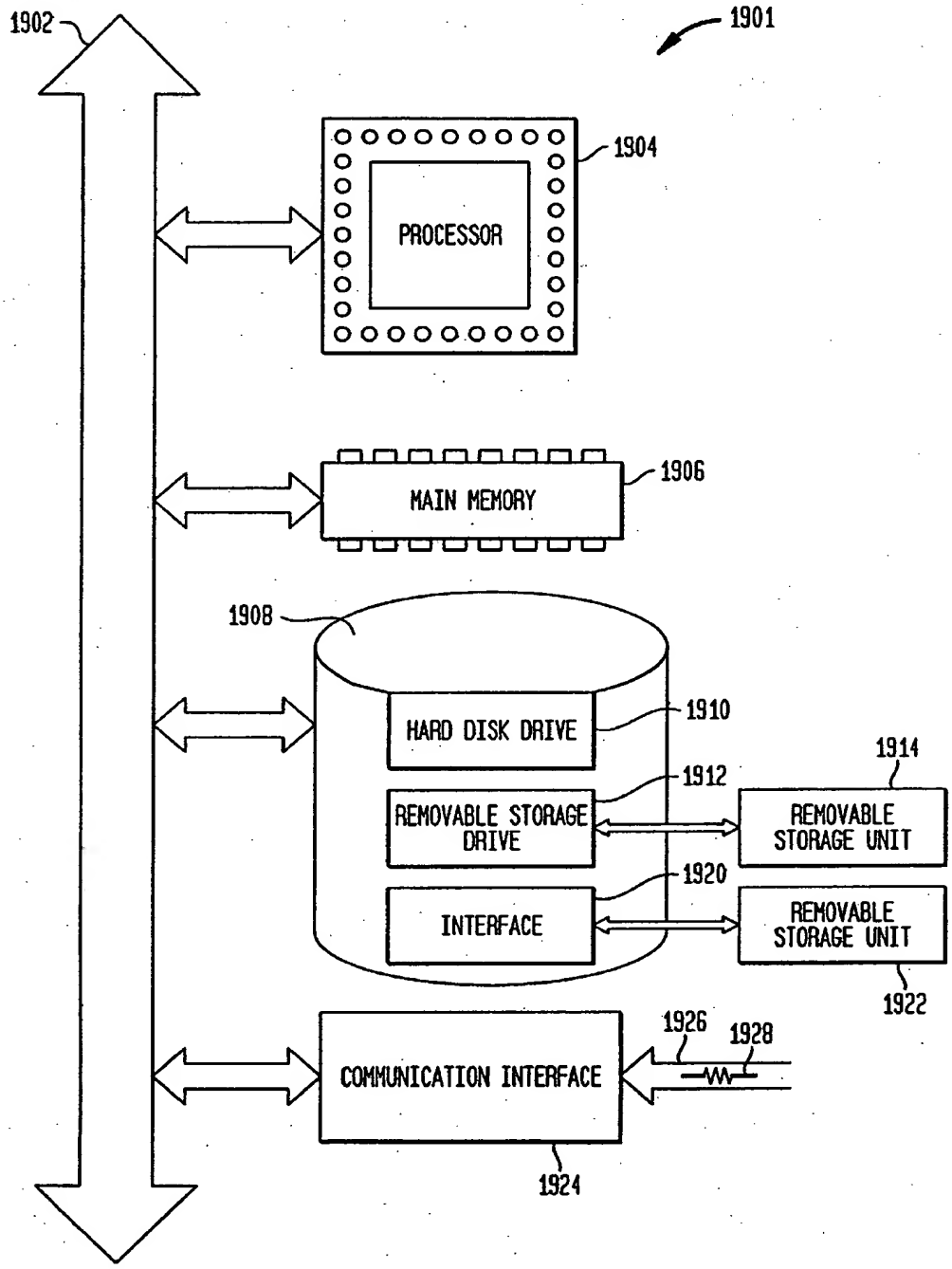
Min 06/03/96
Max 06/12/96
Sat 0
Sun 0

Min 05/29/96 06/14/96
Min

Replacement Sheet
Sheet 33 of 167
Appl. No.: 09/100,088; Filed: June 19, 1998
Dkt No.: 1606.002004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

Appl. No. : 09/100,088; Filed: June 19, 1998
Dkt No. : 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 19



Appl. No. : 09/100,088; Filed: June 19, 1998
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Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 20

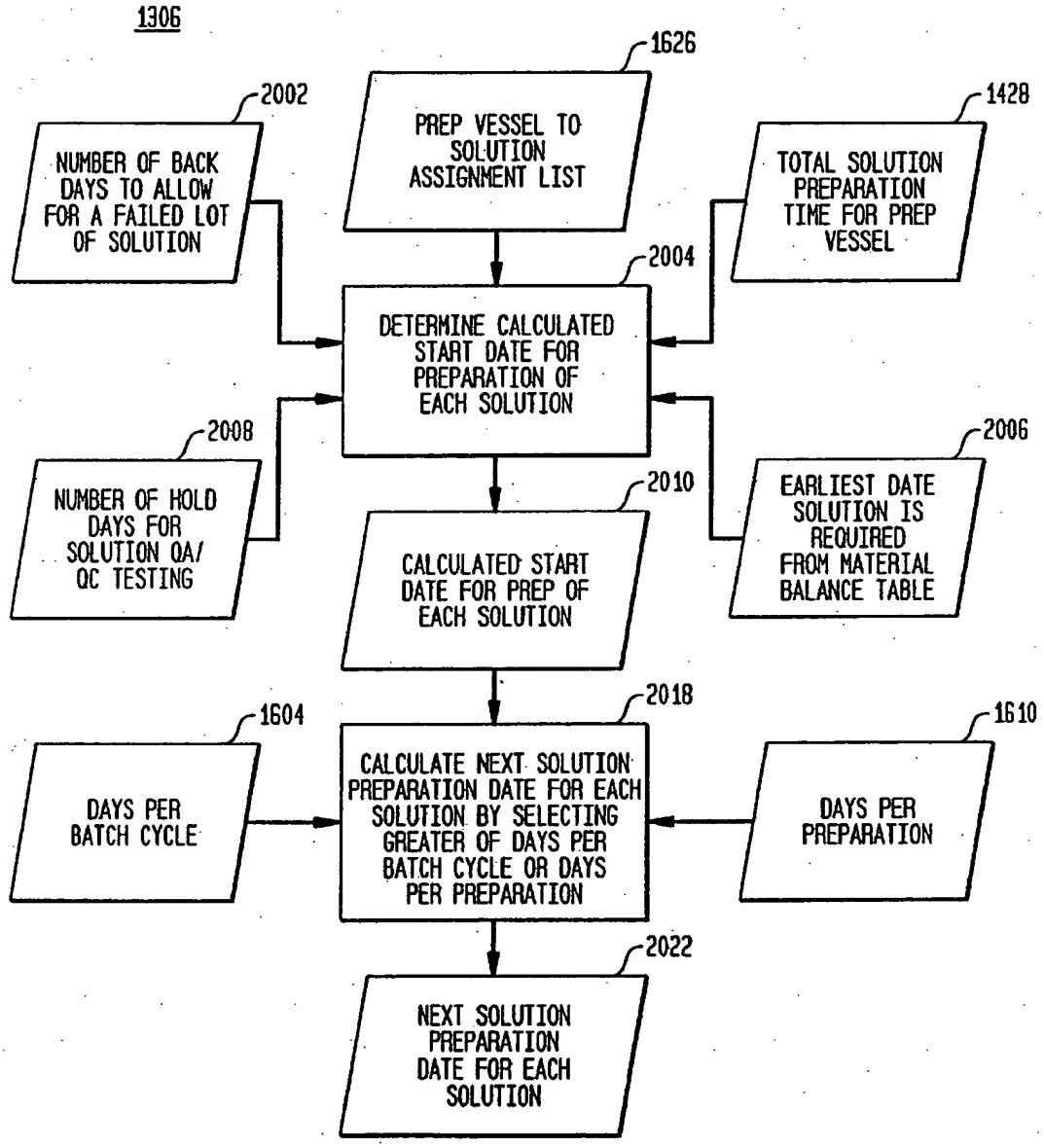

FIG. 21A

	2102 Category/Assay
1	Environmental
2	Temperature
3	Humidity
4	Particle Count
5	
6	Analytical
7	Visual
8	Certificate of Analysis
9	Appearance
10	Chemical
11	Solubility
12	pH
13	Osmolality
14	Water Content(by Karl Fischer)
15	Key Element Analysis(by ICP Atomic Adsorption Spectroscopy)
16	GC/Mass Spec
17	Biochemical
18	DNA
19	DNA Fluorochrome Stain
20	Protein
21	Hemoglobin
22	Electrophoretic Profiles by SDS-PAGE
23	A280
24	Bradford Assay
25	Amino Acid Analysis by HPLC
26	Endotoxin
27	Gel Clot LAL
28	Immunological
29	ELISA
30	Western Blots
31	Activity
32	Chromagenic Substrate Assays
33	
34	In Vitro Biological
35	Microbilogical
36	Mycoplasma(Barile Method)
37	Bacteriophage(Screened)
38	Cell Passage Test
39	Adventitious viral Agents
40	CPE
41	BVD
42	P13
43	IBR
44	Virus Neutralization Titers(9CFR)
45	BVD
46	P13
47	IBR
48	Tritiated Thymidine Uptake in Mouse Cells
49	General Safety Test(Guinea Pigs)
50	
51	

Appl. No. : 09/100,088; Filed: June 19, 1998
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For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 21B

2104 2106

Code	Man Hour			Disp. Material
	Set Up	Per Sample	Clean Up	
E-1	0.5	0.1	0.5	
E-2	0.5	0.1	0.5	
E-3	0.5	0.2	0.5	
AV-1	0.25	0.2	0.5	
AV-2	0.25	0.05	0.25	
AC-1	0.5	0.1	0.5	
AC-2	0.25	0.05	0.25	
AC-3	0.25	0.1	0.25	
AC-4	0.5	0.2	0.5	
AC-5	1	0.25	1	
AC-6	1	0.25	1	
AB-1	0.5	0.1	0.5	
AB-2	0.5	0.1	0.5	
AB-3	1	0.2	1	
AB-4	0.25	0.1	0.25	
AB-5	0.5	0.1	0.5	
AB-6	1	0.25	1	
AB-7	0.5	0.1	0.5	
AI-1	1	0.1	1	
AI-2	1.5	0.2	1.5	
AA-1	1	0.1	1	
VB-1	0.5	0.2	0.5	
VB-2	0.5	0.2	0.5	
VB-3	0.5	0.2	0.5	
VB-4	1	0.2	1	
	2	0.2	1	
VB-5	2	0.2	1	
VB-6	2	0.2	1	
VB-7	2	0.2	1	
VB-8	2	0.2	1	
VB-9	2	0.2	1	
VB-10	2	0.2	1	
VB-11	2	0.2	1	
VB-12	2	0.2	1	
VB-13	1	0.2	1	

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(As Amended)

FIG. 22

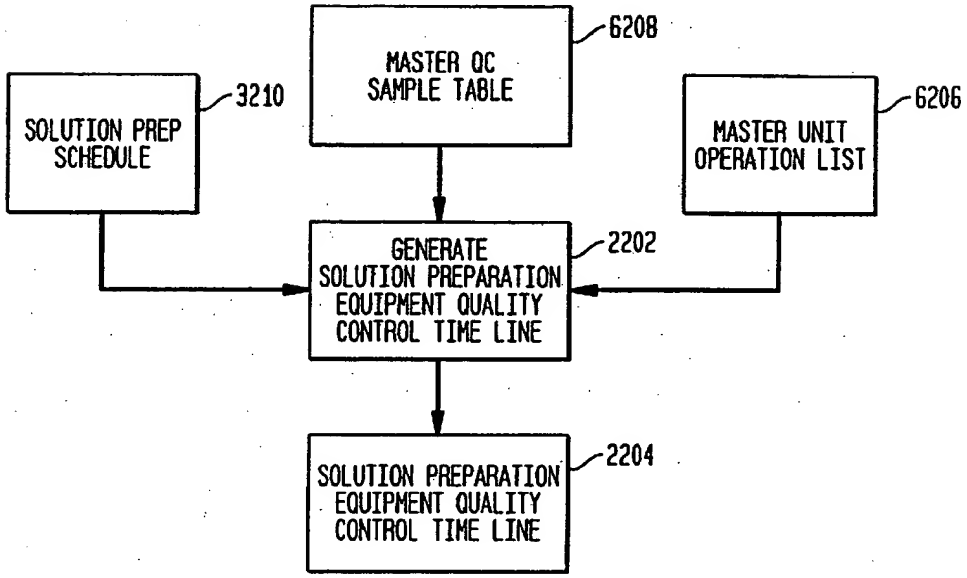
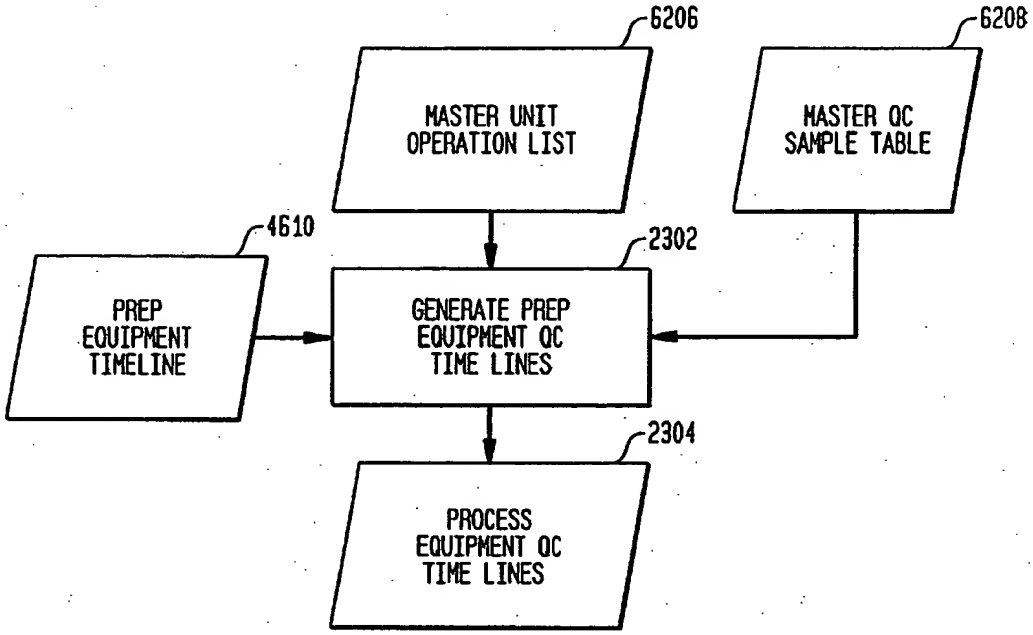


FIG. 23



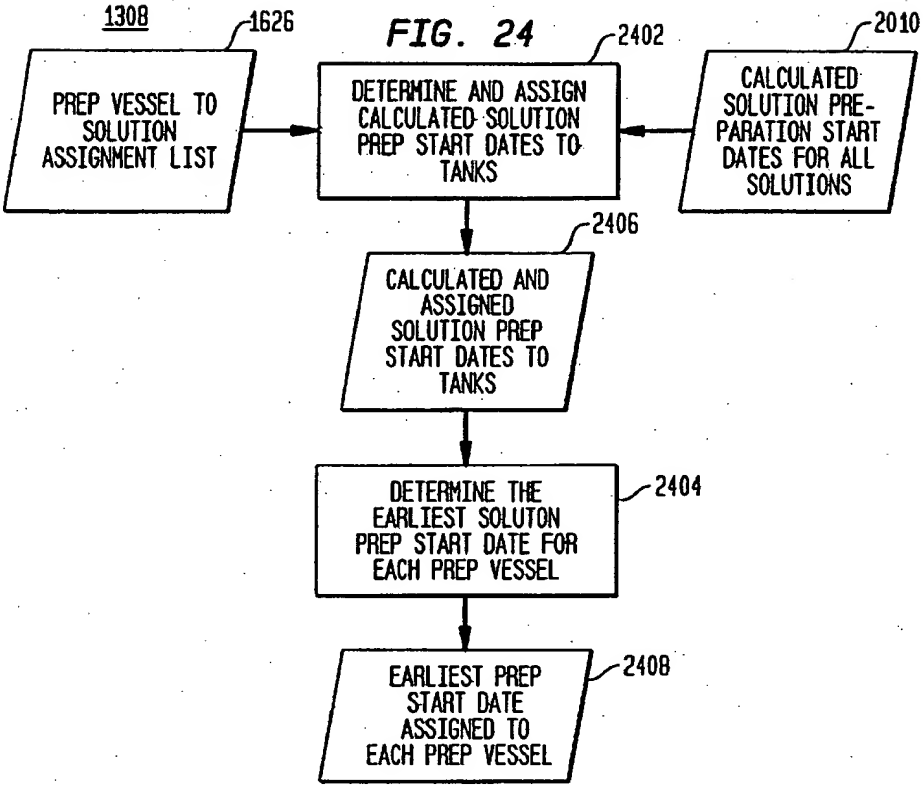

1308
1626
PREP VESSEL TO SOLUTION ASSIGNMENT LIST
2402
DETERMINE AND ASSIGN CALCULATED SOLUTION PREP START DATES TO TANKS
2010
CALCULATED SOLUTION PRE-PARATION START DATES FOR ALL SOLUTIONS
2406
CALCULATED AND ASSIGNED SOLUTION PREP START DATES TO TANKS
2404
DETERMINE THE EARLIEST SOLUTON PREP START DATE FOR EACH PREP VESSEL
2408
EARLIEST PREP START DATE ASSIGNED TO EACH PREP VESSEL

FIG. 24

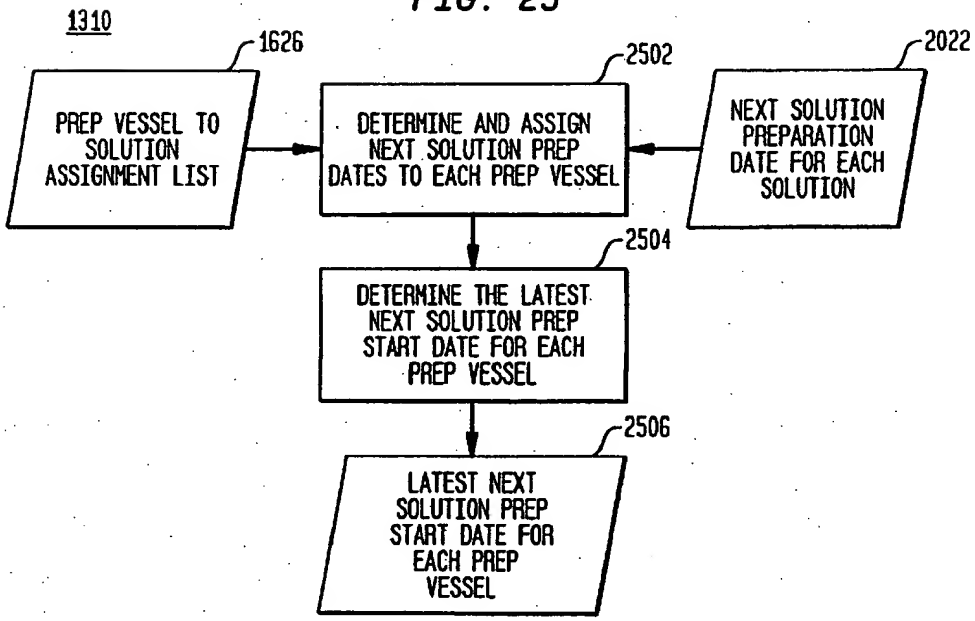

1310
1626
PREP VESSEL TO SOLUTION ASSIGNMENT LIST
2502
DETERMINE AND ASSIGN NEXT SOLUTION PREP DATES TO EACH PREP VESSEL
2022
NEXT SOLUTION PREPARATION DATE FOR EACH SOLUTION
2504
DETERMINE THE LATEST NEXT SOLUTION PREP START DATE FOR EACH PREP VESSEL
2506
LATEST NEXT SOLUTION PREP START DATE FOR EACH PREP VESSEL

FIG. 25

Appl. No. : 09/100,088; Filed: June 19, 1998
Dkt No. : 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 26

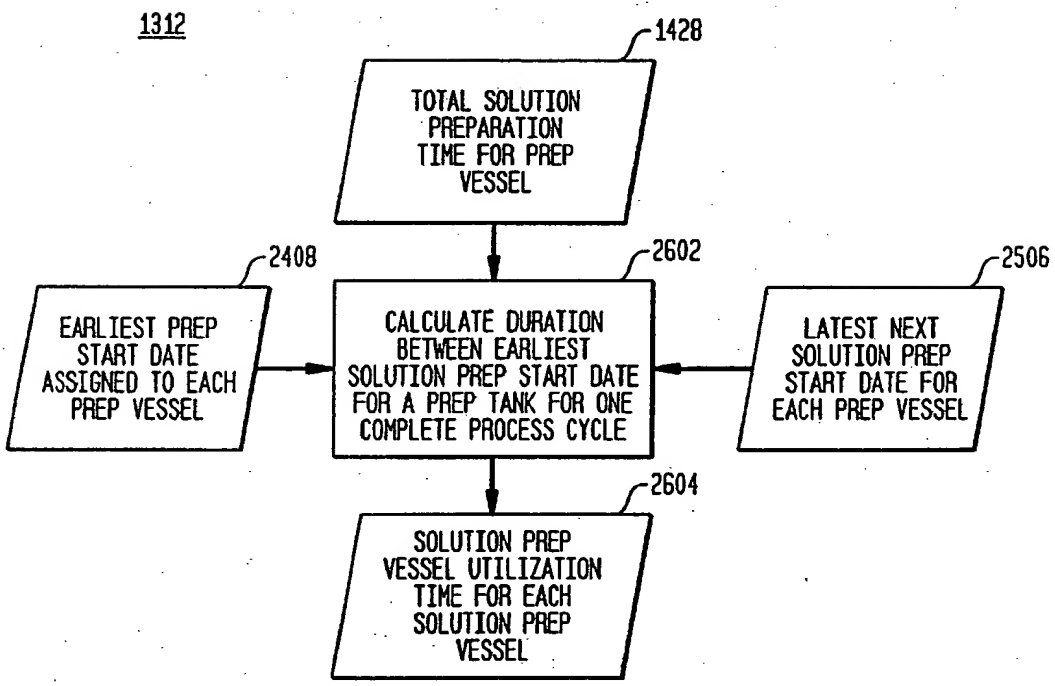


FIG. 27

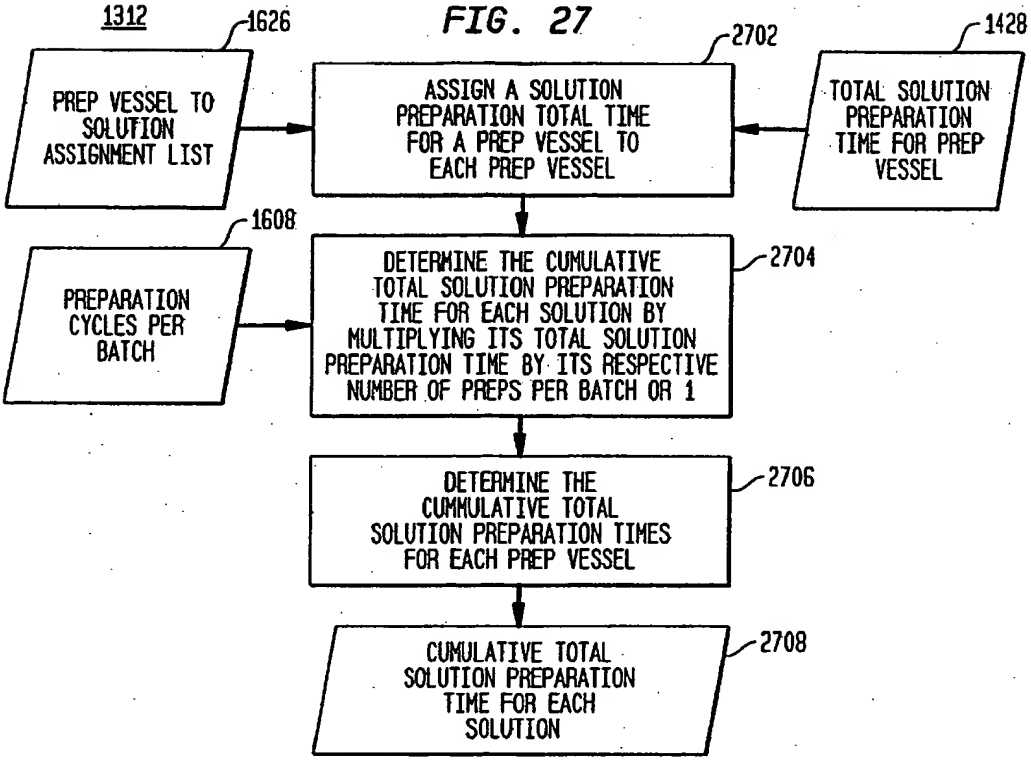
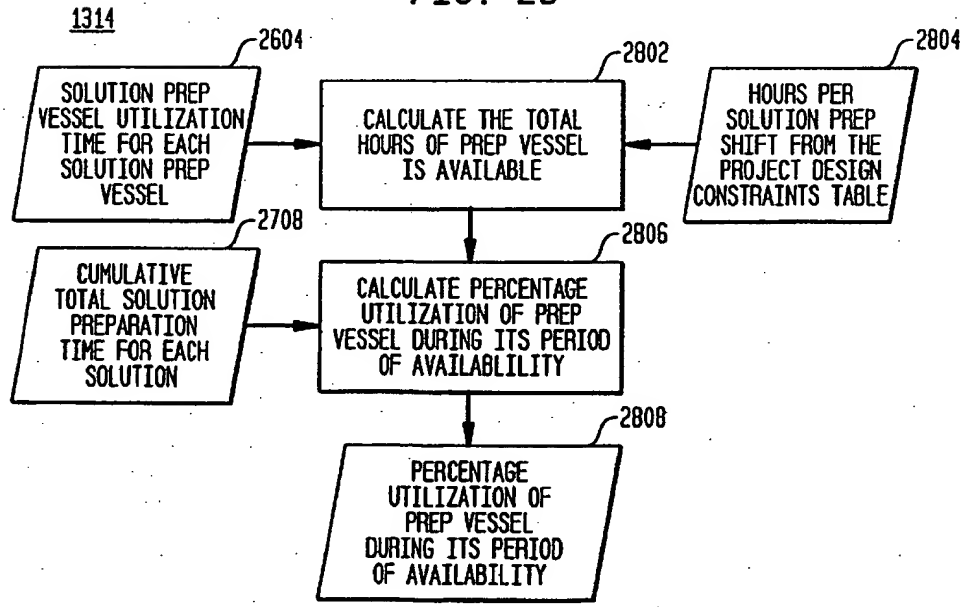

1312
1626
PREP VESSEL TO SOLUTION ASSIGNMENT LIST
2702
ASSIGN A SOLUTION PREPARATION TOTAL TIME FOR A PREP VESSEL TO EACH PREP VESSEL
1428
TOTAL SOLUTION PREPARATION TIME FOR PREP VESSEL
1608
PREPARATION CYCLES PER BATCH
2704
DETERMINE THE CUMULATIVE TOTAL SOLUTION PREPARATION TIME FOR EACH SOLUTION BY MULTIPLYING ITS TOTAL SOLUTION PREPARATION TIME BY ITS RESPECTIVE NUMBER OF PREPS PER BATCH OR 1
2706
DETERMINE THE CUMMULATIVE TOTAL SOLUTION PREPARATION TIMES FOR EACH PREP VESSEL
2708
CUMULATIVE TOTAL SOLUTION PREPARATION TIME FOR EACH SOLUTION

FIG. 28


1314
2604
SOLUTION PREP VESSEL UTILIZATION TIME FOR EACH SOLUTION PREP VESSEL
2802
CALCULATE THE TOTAL HOURS OF PREP VESSEL IS AVAILABLE
2804
HOURS PER SOLUTION PREP SHIFT FROM THE PROJECT DESIGN CONSTRAINTS TABLE
2708
CUMULATIVE TOTAL SOLUTION PREPARATION TIME FOR EACH SOLUTION
2806
CALCULATE PERCENTAGE UTILIZATION OF PREP VESSEL DURING ITS PERIOD OF AVAILABLILITY
2808
PERCENTAGE UTILIZATION OF PREP VESSEL DURING ITS PERIOD OF AVAILABILITY

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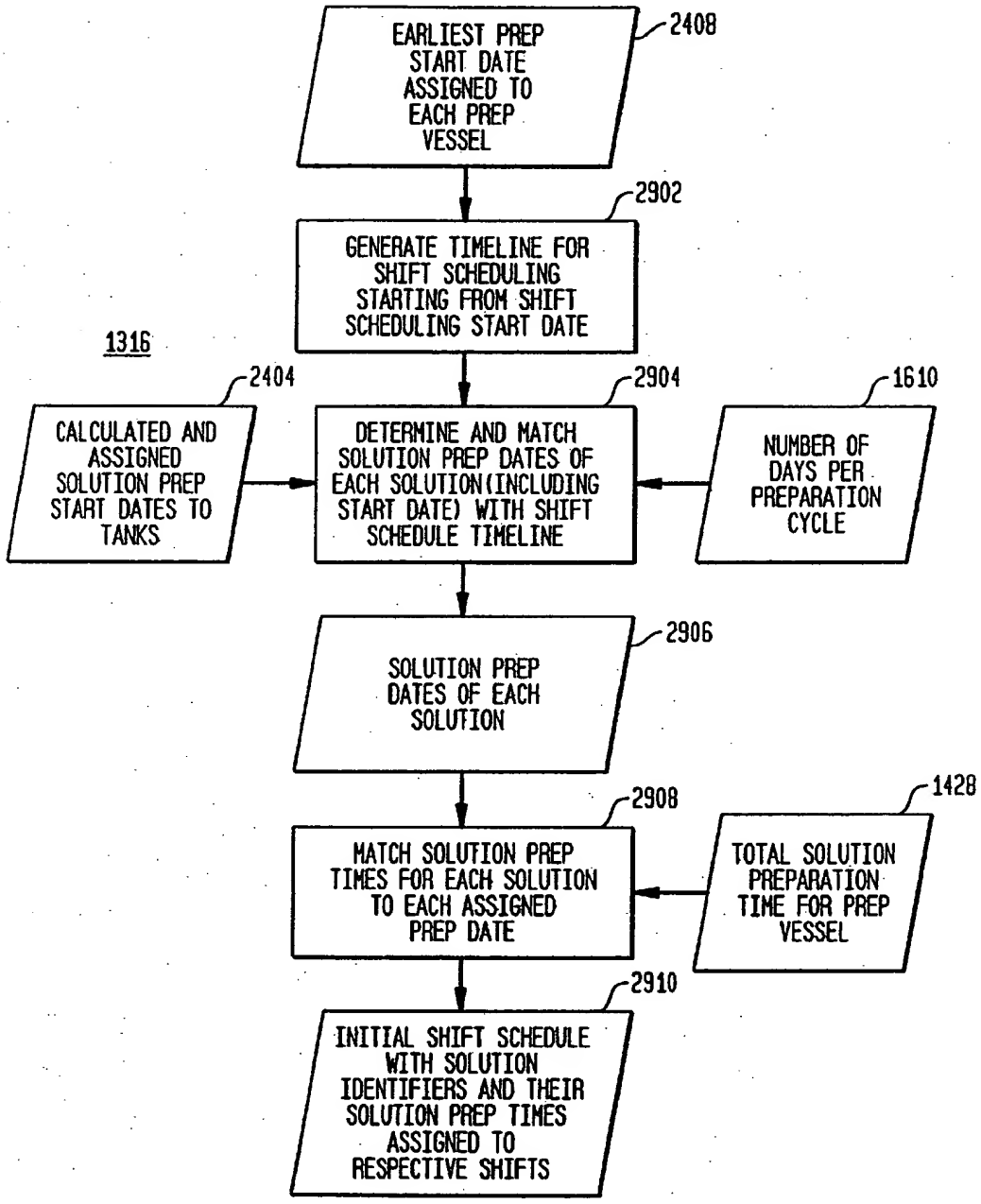
For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 29



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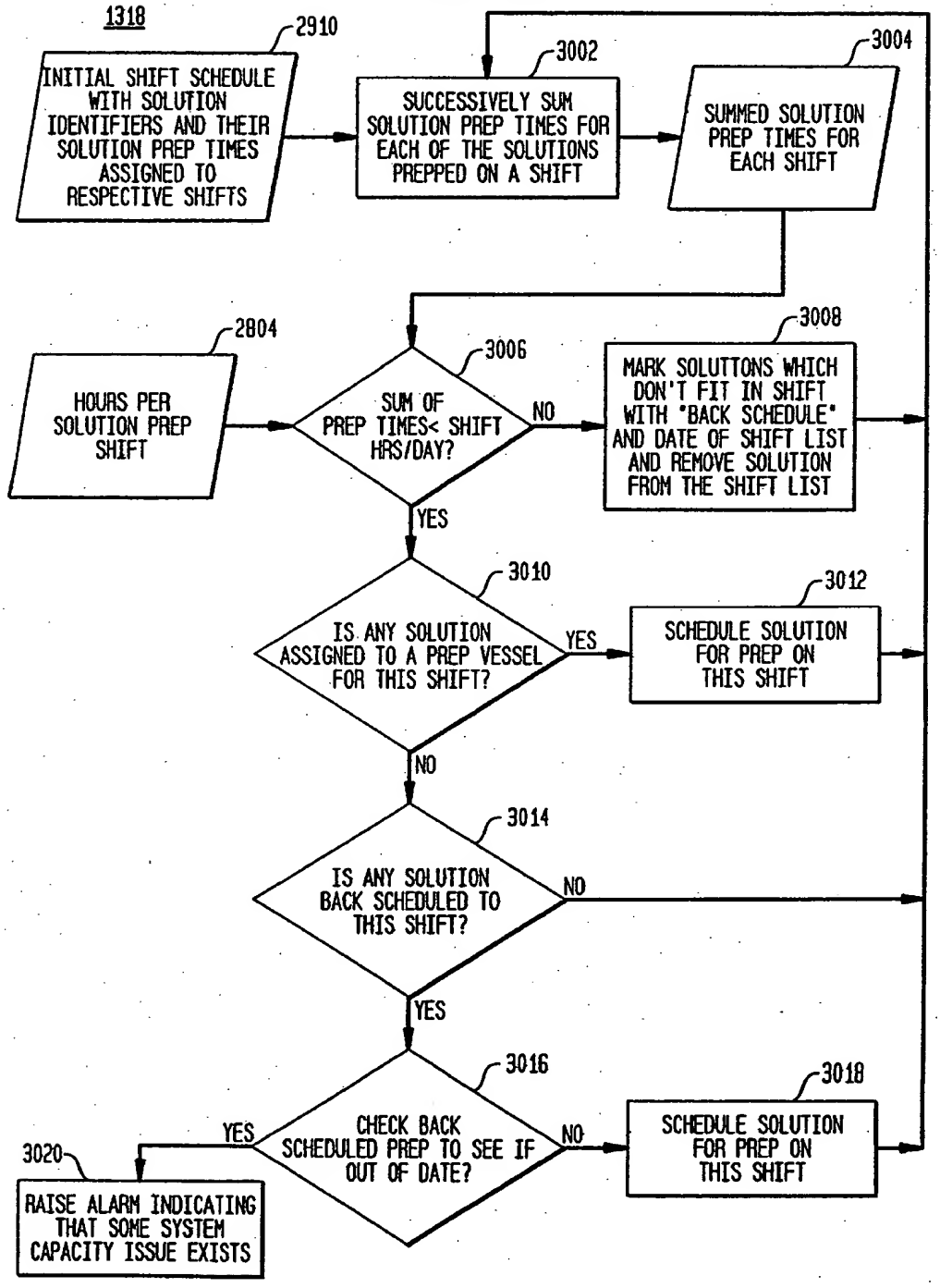
For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 30



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For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 31A

2804

			8 Hrs/Day	59		60		61		62	
Tank 101	Usage	3.5	06/13/96 04/05/96	06/03/96		06/04/96		06/05/96		06/06/96	
Soln.		Period	Start	Date	Hrs.	Date	Hrs.	Date	Hrs.	Date	Hrs.
S-0101											
S-0102	13.2	56	02/14/96	04/10/96		04/10/96		06/05/96	3.5	06/05/96	
S-0103	1.7	7	05/22/96	05/29/96		05/29/96		06/05/96	3.5	06/05/96	
S-0104	8.3	7	05/22/96	05/29/96		05/29/96		06/05/96	3.5	06/05/96	
S-0105	8.3	7	05/22/96	05/29/96		05/29/96		06/05/96	3.5	06/05/96	
S-0106											
S-0107											
S-0108											
S-0109	22.2	7	05/29/96	05/29/96		05/29/96		06/05/96	3.5	06/05/96	
S-0111											
S-0112											
S-0113											
S-0114											
S-0115											
S-0116											
S-0117											
S-0118											
S-0119											
S-0120											
S-0121											
S-0122	0.0	7	05/29/96	05/29/96		05/29/96		06/05/96	3.5	06/05/96	
					0		0		21		0

3102 1610 2906

FIG. 31B

63		64		65		66		67		68	
06/07/96		06/08/96		06/09/96		06/10/96		06/11/96		06/12/96	
Date	Hrs.	Date	Hrs.	Date	Hrs.	Date	Hrs.	Date	Hrs.	Date	Hrs.
06/05/96		06/05/96		06/05/96		06/05/96		06/05/96		06/05/96	
06/05/96		06/05/96		06/05/96		06/05/96		06/05/96		06/12/96	3.5
06/05/96		06/05/96		06/05/96		06/05/96		06/05/96		06/12/96	3.5
06/05/96		06/05/96		06/05/96		06/05/96		06/05/96		06/12/96	3.5
06/05/96		06/05/96		06/05/96		06/05/96		06/05/96		06/12/96	3.5
06/05/96		06/05/96		06/05/96		06/05/96		06/05/96		06/12/96	3.5
	0		0		0		0		0		17.5

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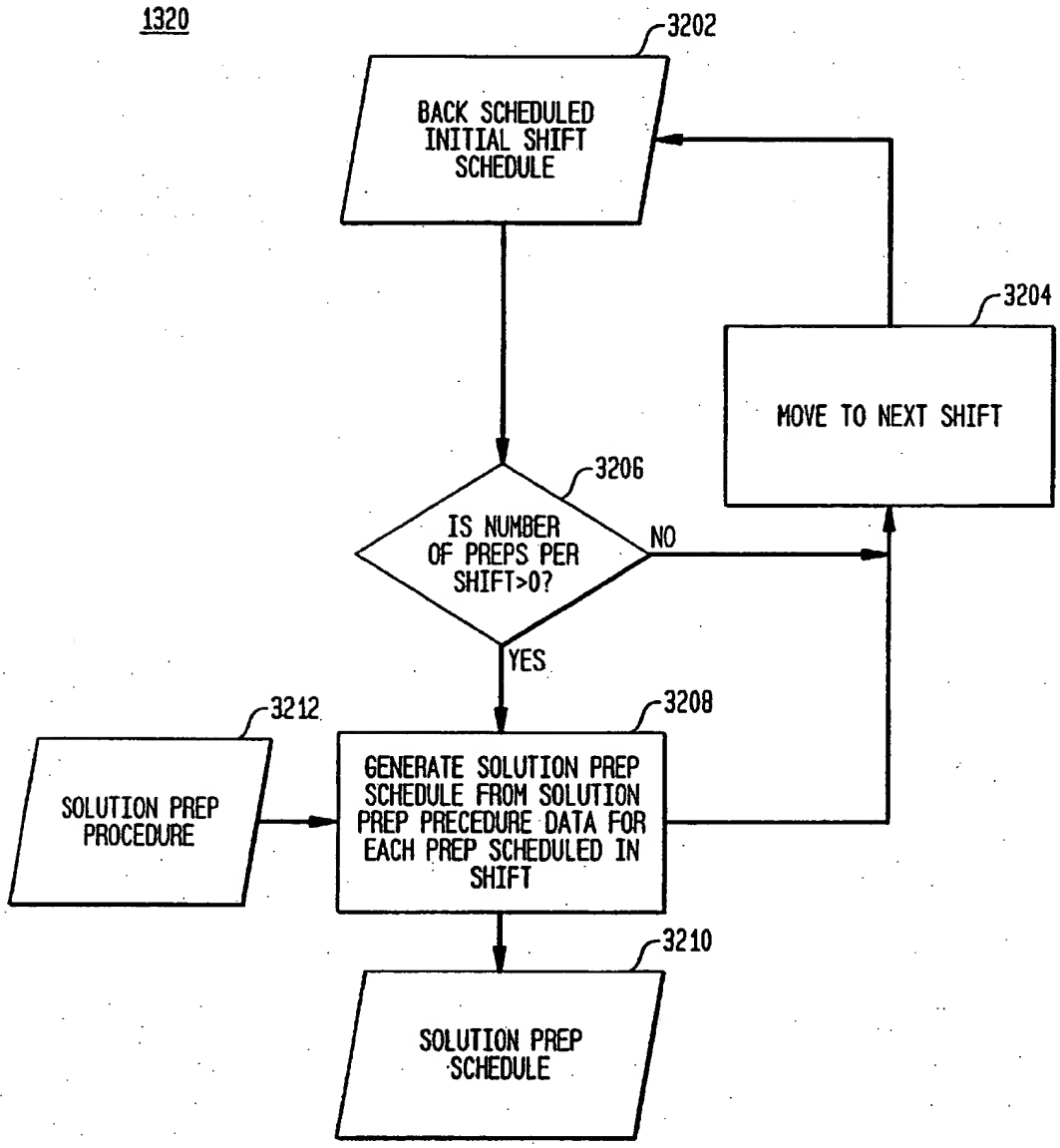
For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 32



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(As Amended)

FIG. 33

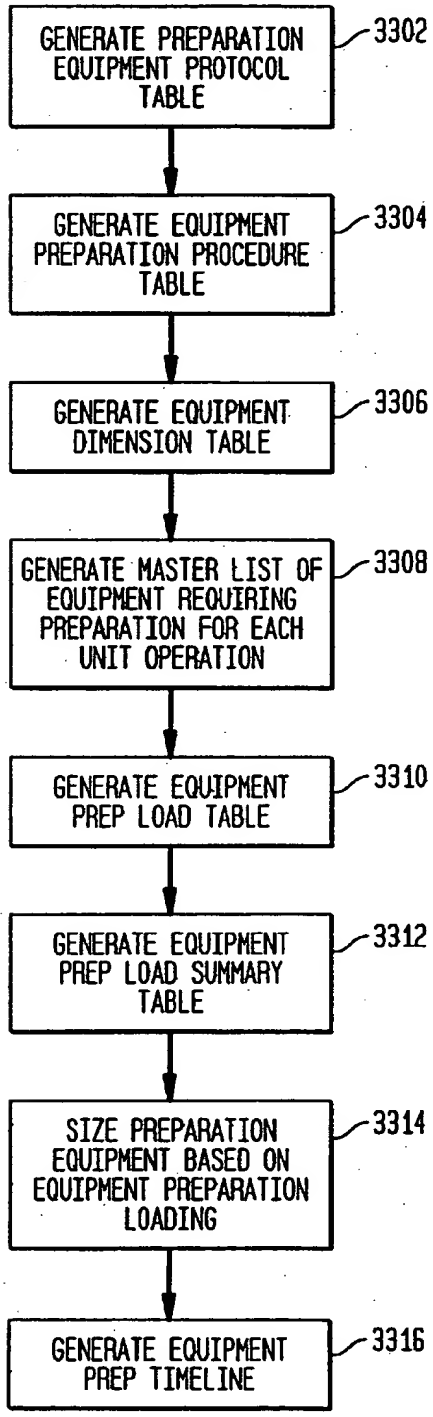

FIG. 34

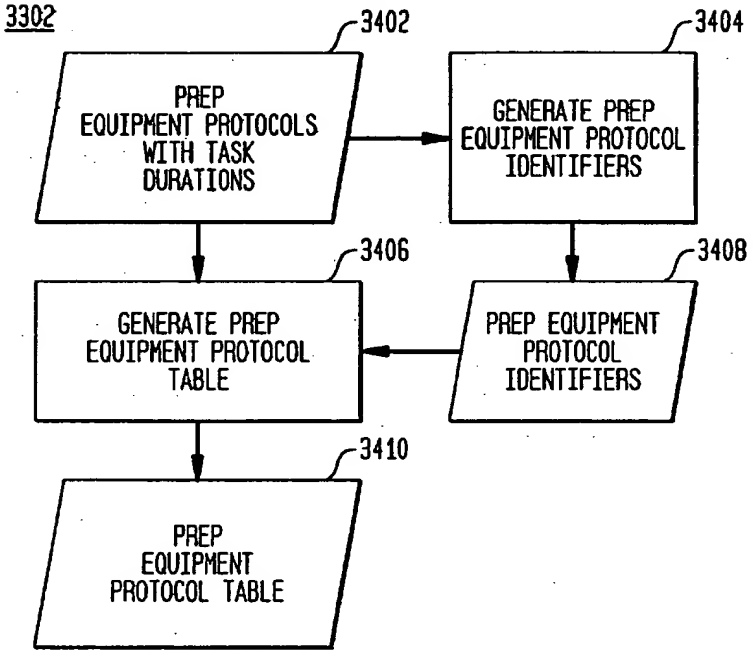
3302
3402
PREP EQUIPMENT PROTOCOLS WITH TASK DURATIONS
3404
GENERATE PREP EQUIPMENT PROTOCOL IDENTIFIERS
3406
GENERATE PREP EQUIPMENT PROTOCOL TABLE
3408
PREP EQUIPMENT PROTOCOL IDENTIFIERS
3410
PREP EQUIPMENT PROTOCOL TABLE

FIG. 35

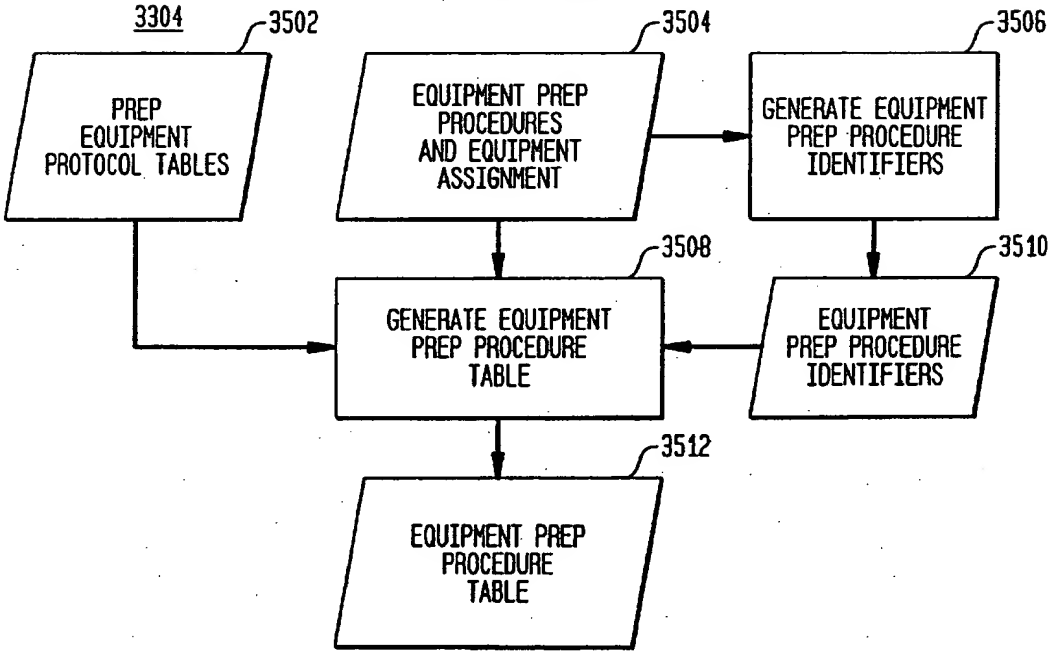
3304
3502
PREP EQUIPMENT PROTOCOL TABLES
3504
EQUIPMENT PREP PROCEDURES AND EQUIPMENT ASSIGNMENT
3506
GENERATE EQUIPMENT PREP PROCEDURE IDENTIFIERS
3508
GENERATE EQUIPMENT PREP PROCEDURE TABLE
3510
EQUIPMENT PREP PROCEDURE IDENTIFIERS
3512
EQUIPMENT PREP PROCEDURE TABLE

FIG. 36A

PREP EQUIPMENT PROTOCOL-BENCH SINK

3408

	CYCLE CODE	MINUTES/CYCLE										TOTAL
		LOAD	PRE WASH RINSE		DETERGENT WASH			POST WASH RINSE		FINAL RINSE	HOLD/ DRY	
			NPHW	NPCW	MINUTES	REAGENT	Gm/CF	NPHW	NPCW			
1	BS-1	5	2	2	5	Alconox	0.5	2	2	2		20
2	BS-2	5	2	2	5	Alconox	0.5	2	2	2		20
3	BS-3	5	2	2	5	Alconox	0.5	2	2	2		20
4	BS-4	5	2	2	5	Alconox	0.5	2	2	2		20
5	BS-5	5	2	2	5	Alconox	0.5	2	2	2		20

3602 3604

FIG. 36B

PREP EQUIPMENT PROTOCOL-WASH STATION

3408

	PROTOCOL CODE	MINUTES/CYCLE									TOTAL
		LOAD	PRE WASH RINSE		DETERGENT WASH			POST WASH RINSE		FINAL RINSE	
			NPHW	NPCW	MINUTES	REAGENT	Gm/CF	NPHW	NPCW		
1	WS-1	5	2	2	5	Alconox	0.5	2	2	2	15
2	WS-2	5	2	2	5	Alconox	0.5	2	2	2	15
3	WS-3	5	2	2	5	Alconox	0.5	2	2	2	15
4	WS-4	5	2	2	5	Alconox	0.5	2	2	2	15
5	WS-5	5	2	2	5	Alconox	0.5	2	2	2	15

FIG. 36C

PREP EQUIPMENT PROTOCOL-GLASSWARE WASHER

3408

	CYCLE CODE	MINUTES/CYCLE										TOTAL
		LOAD	PRE WASH RINSE		DETERGENT WASH			POST WASH RINSE		FINAL RINSE	UNLOAD	
			NPHW	NPCW	MINUTES	REAGENT	Gm/CF	NPHW	NPCW			
1	GW-1	15	2	2	5	Alconox	0.5	2	2	2	10	40
2	GW-2	15	2	2	5	Alconox	0.5	2	2	2	10	40
3	GW-3	15	2	2	5	Alconox	0.5	2	2	2	10	40
4	GW-4	15	2	2	5	Alconox	0.5	2	2	2	10	40
5	GW-5	15	2	2	5	Alconox	0.5	2	2	2	10	40

FIG. 36D

PREP EQUIPMENT PROTOCOL-GLASSWARE DRYER

3408

	CYCLE CODE	LOAD	HEAT UP MINUTES	DRY		COOL MINUTES	UNLOAD	TOTAL
				TEMP(C)	MINUTES			
1	DO-1	10	30	250	40	30	10	120
2	DO-2	10	30	250	25	30	10	105
3	DO-3	10	30	250	25	30	10	105
4	DO-4	10	30	250	25	30	10	105
5	DO-5	10	30	250	25	30	10	105

3618 3620 3622 3624 3626 3628

FIG. 36E

PREP EQUIPMENT PROTOCOL-CARBOY WASHER

3408

	CYCLE CODE	MINUTES/CYCLE										TOTAL
		LOAD	PRE WASH RINSE		DETERGENT			POST WASH RINSE		FINAL RINSE	UNLOAD	
			NPHW	NPCW	MINUTES	REAGENT	Gm/CF	NPHW	NPCW			
1	CW-1	15	2	2	5	Alconox	0.5	2	2	2	15	15
2	CW-2	15	2	2	5	Alconox	0.5	2	2	2	15	15
3	CW-3	15	2	2	5	Alconox	0.5	2	2	2	15	15
4	CW-4	15	2	2	5	Alconox	0.5	2	2	2	15	15
5	CW-5	15	2	2	5	Alconox	0.5	2	2	2	15	15

FIG. 36F

PREP EQUIPMENT PROTOCOL-CARBOY DRYER

3408

	CYCLE CODE	LOAD	HEAT UP MINUTES	DRY		COOL MINUTES	UNLOAD	TOTAL
				TEMP(C)	MINUTES			
1	CD-1	10	30	250	40	30	10	100
2	CD-2	10	30	250	25	30	10	85
3	CD-3	10	30	250	25	30	10	85
4	CD-4	10	30	250	25	30	10	85
5	CD-5	10	30	250	25	30	10	85

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(As Amended)

FIG. 36G-1

Prep Equipment Protocol-Steam Sterilizer

	3606	3608	3610	3612	3614	3616
		Cycles				
		SS-1				
		Press (Bar)	Minutes To Ach.	Minutes To Hold	No. of Cycles	Subt.
1	Load					20
2						
3	Pre Sterilization					
4	Deep Vacuum		15	1	1	16
5	Vacuum/Steam Pulse					
6	Vacuum					
7	Steam					
8	Subtotal					16
9						
10	Sterilization					
11	Steam	1	20	40	1	60
12	Steam/Air					
13	Subtotal					60
14						
15	Cooling					
16	Direct Air Cooling					
17	Indirect Jacket Cooling	0	40	0	1	40
18	Overpressure					
19	Subtotal					40
20						
21	Drying					
22	Fast Exhaust	0	20	5	1	25
23	Slow Exhaust					
24	Deep Vacuum					
25	Vacuum Pulse					
26	Heat					
27	Heated Pressure					
28	Subtotal					25
29						
30	Unload					20
31						
32	Total Minutes					161
33	Total Hours					2.7

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(As Amended)

FIG. 36G-2

	SS-2					SS-3				
	Press (Bar)	Minutes To Ach.	Minutes To Hold	No. of Cycles	Subt.	Press (Bar)	Minutes To Ach.	Minutes To Hold	No. of Cycles	Subt.
					20					20
	1	3 2	0 0	9 9	27 18 45	1	3 2	0 0	9 9	27 18 45
	1	20	40	1	60 60	1	20	40	1	60 60
	0	40	0	1	40 40	0 1	40 40	0 0	1 1	40 40 80
		3	0	10	30 30	0	20	5	1	25 25
					20					20
					195					230
					3.3					3.8

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(As Amended)

FIG. 36H

3408

PREP EQUIPMENT PROTOCOL-DRY HEAT STERILIZER

	CYCLE CODE	LOAD	HEAT UP MINUTES	STERILIZATION		COOL MINUTES	UNLOAD	TOTAL
				TEMP(C)	MINUTES			
1	SO-1	15	30	250	40	30	15	130
2	SO-2	15	30	250	25	30	15	115
3	SO-3	15	30	250	25	30	15	115
4	SO-4	15	30	250	25	30	15	115
5	SO-5	15	30	250	25	30	15	115

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(As Amended)

FIG. 37A

Equipment Prep Procedures

3706 3702 3704

			EPC1	EPC2	EPC3	EPC4	EPC5	EPC6	EPC7
1	Initial Rinse								
2									
3	Bench Sink-1								
4	Protocol		BS-1	BS-1	BS-2	BS-1			
5	Duration	PHrs.	0.33	0.33	0.33	0.33			
6	Hold/Dry	PHrs.	0	0	0				
7	Subtotal	PHrs.	0.33	0.33	0.33	0.33	0.00	0.00	0.00
8	Cummulative	PHrs.	0.33	0.33	0.33	0.33	0.00	0.00	0.00
9									
10	Wash Station-1								
11	Protocol						WS-1	WS-1	
12	Duration	PHrs.					0.25	0.25	
13	Hold/Dry	PHrs.							
14	Subtotal	PHrs.	0.00	0.00	0.00	0.00	0.25	0.25	0.00
15	Cummulative	PHrs.	0.33333	0.33333	0.33333	0.33333	0	0	0
16									
17	Cleaning								
18									
19	Bench Sink-1								
20	Protocol		BS-3	BS-3	BS-4				
21	Duration	PHrs.	0.33	0.33	0.33				
22	Hold/Dry	PHrs.							
23	Subtotal	PHrs.	0.33	0.33	0.33	0.00	0.00	0.00	0.00
24	Cummulative	PHrs.	0.66667	0.66667	0.66667	0.33333	0	0	0
25									
26	Glassware Washer-1								
27	Protocol					GW-1			
28	Duration	PHrs.				0.67			
29	Hold/Dry	PHrs.							
30	Subtotal	PHrs.	0.00	0.00	0.00	0.67	0.00	0.00	0.00
31	Cummulative	PHrs.	0.66667	0.66667	0.66667	1	0	0	0
32									
33	Glassware Dryer-1								
34	Protocol		GD-1	GD-1	GD-2	GD-3			
35	Duration	PHrs.	2.00	2.00	1.75	1.75			
36	Hold/Dry	PHrs.							
37	Subtotal	PHrs.	2.00	2.00	1.75	1.75	0.00	0.00	0.00
38	Cummulative	PHrs.	2.66667	2.66667	2.41667	2.75	0	0	0
39									
40	Carboy Washer-1								
41	Protocol						CW-1	CW-1	
42	Duration	PHrs.					0.25	0.25	
43	Hold/Dry	PHrs.							
44	Subtotal	PHrs.	0.00	0.00	0.00	0.00	0.25	0.25	0.00

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(As Amended)

FIG. 37B

Equipment Prep Procedures

			EPC1	EPC2	EPC3	EPC4	EPC5	EPC6	EPC7
45	Cumulative	PHrs.	2.66667	2.66667	2.41667	2.75	0.25	0.25	0
46									
47	Carboy Dryer-1								
48	Protocol						CD-1	CD-1	
49	Duration	PHrs.					1.67	1.67	
50	Hold/Dry	PHrs.							
51	Subtotal	PHrs.	0.00	0.00	0.00	0.00	1.67	1.67	0.00
52	Cumulative	PHrs.	2.66667	2.66667	2.41667	2.75	1.91667	1.91667	0
53									
54	Prep								
55									
56	Staffing		2	2	2	2	2	2	2
57									
58	Preassembly								
59	Man Hours	MHrs.		1					
60	Procedure Hours			0.5					
61	Cumulative	PHrs.	2.66667	3.16667	2.41667	2.75	1.91667	1.91667	0
62									
63	Wrap								
64	Man Hours	MHrs.	1.5	1.5	1.5	1.5	1.5	1.5	1.5
65	Procedure Hours		0.75	0.75	0.75	0.75	0.75	0.75	0.75
66	Cumulative	PHrs.	3.41667	3.91667	3.16667	3.5	2.66667	2.66667	0.75
67									
68	Sterilization								
69									
70	Autoclave-1								
71	Procedure		SS-1	SS-1	SS-1	SS-1	SS-2		SS-3
72	Duration	PHrs.	2.68	2.68	2.68	2.68	3.25		3.83
73	Hold/Dry	PHrs.							
74	Subtotal	PHrs.	2.68	2.68	2.68	2.68	3.25	0.00	3.83
75	Cumulative	PHrs.	6.10	6.60	5.85	6.18	5.92	2.67	4.58
76									
77	Dry Heat-1								
78	Procedure							SD-1	
79	Hours/Load	PHrs.						2.17	
80	Hold/Dry	PHrs.							
81	Subtotal	PHrs.	0.00	0.00	0.00	0.00	0.00	2.17	0.00
82	Cumulative	PHrs.	6.10	6.60	5.85	6.18	5.92	4.83	4.58
83									
84	Total		6.10	6.60	5.85	6.18	6.17	5.08	4.58
85									
86	Max		2.68	2.68	2.68	2.68	3.25	2.17	3.83

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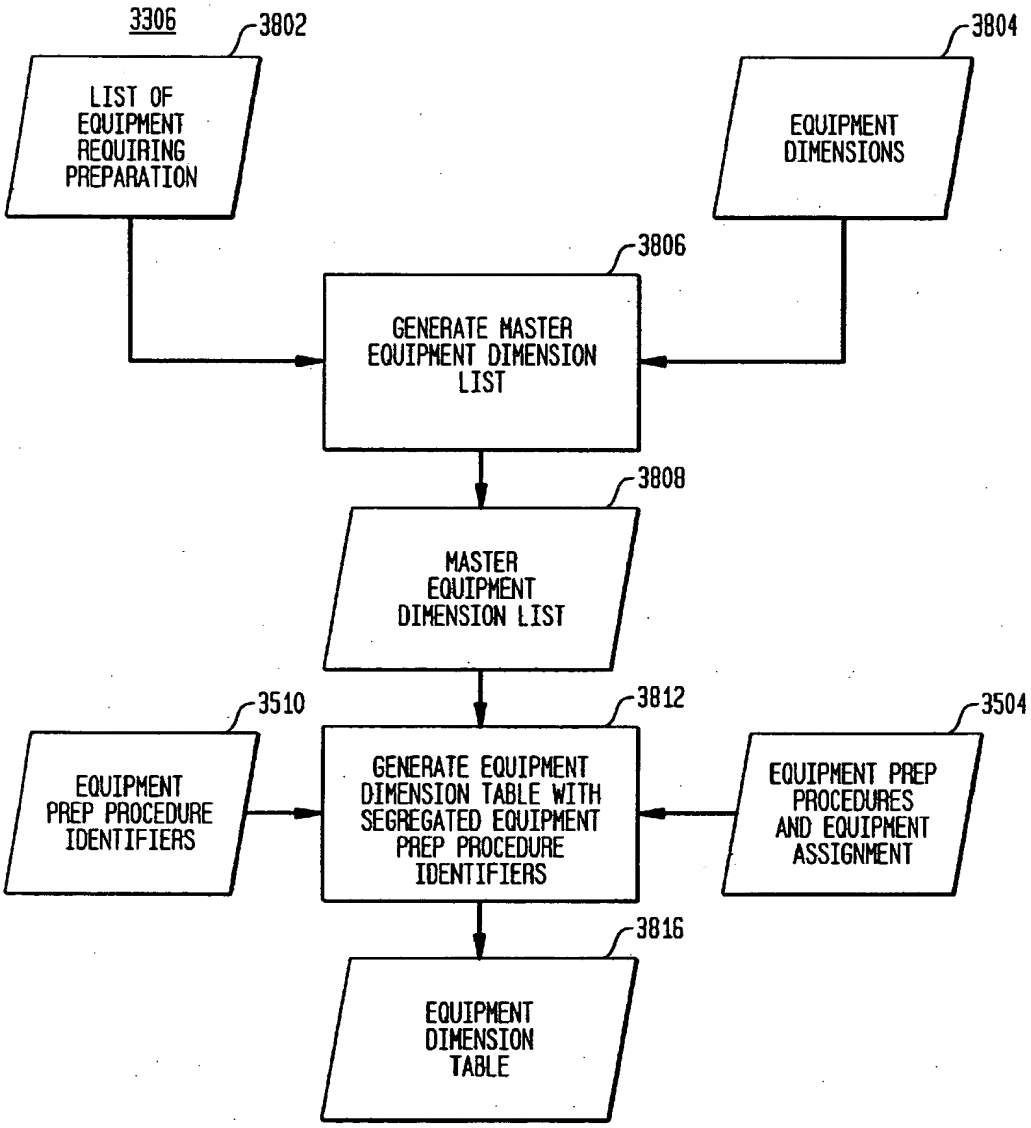
(As Amended)

FIG. 38



Appl. No. : 09/100,088; Filed: June 19, 1998
Dkt No. : 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 39

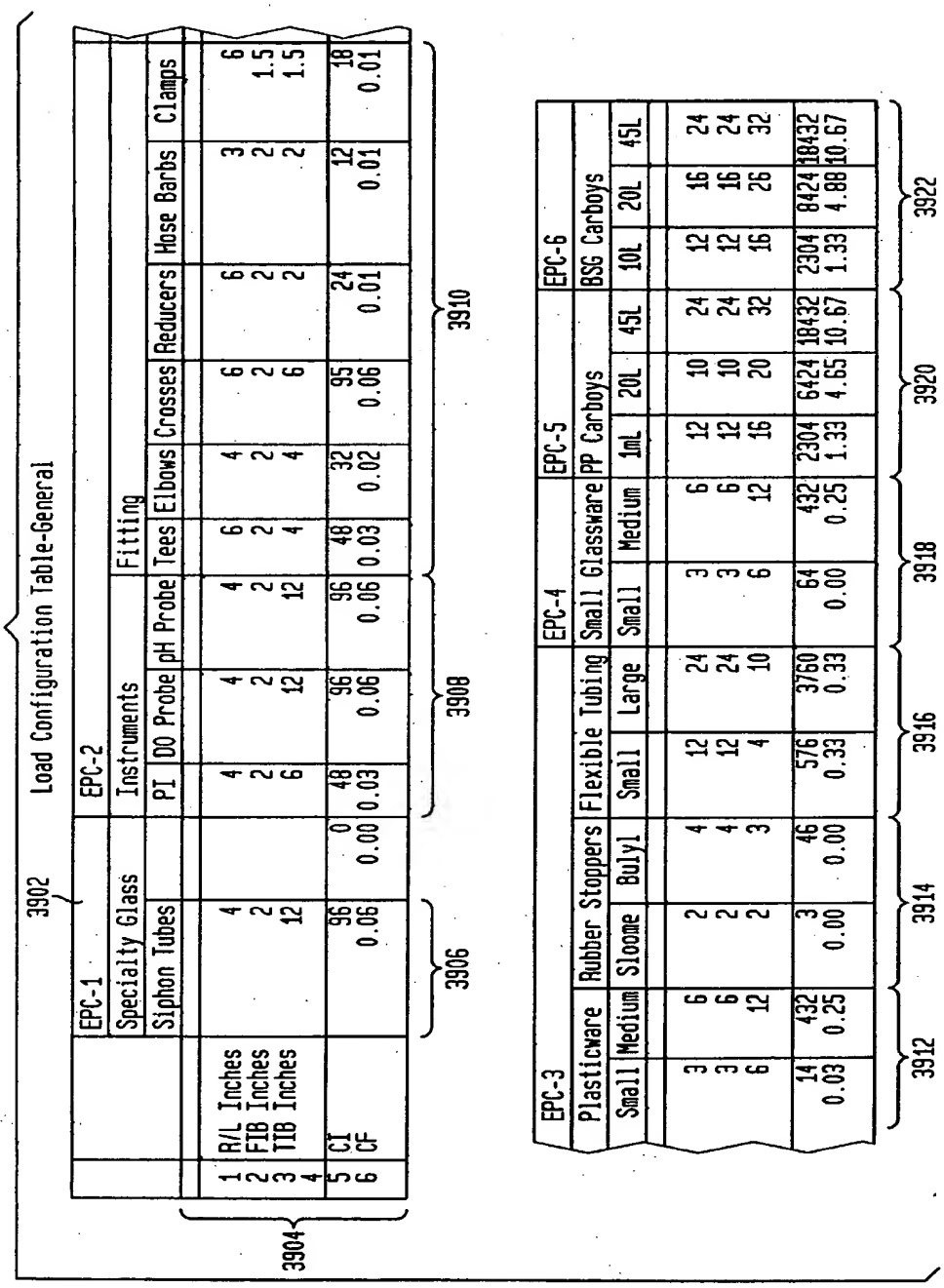


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FIG. 40

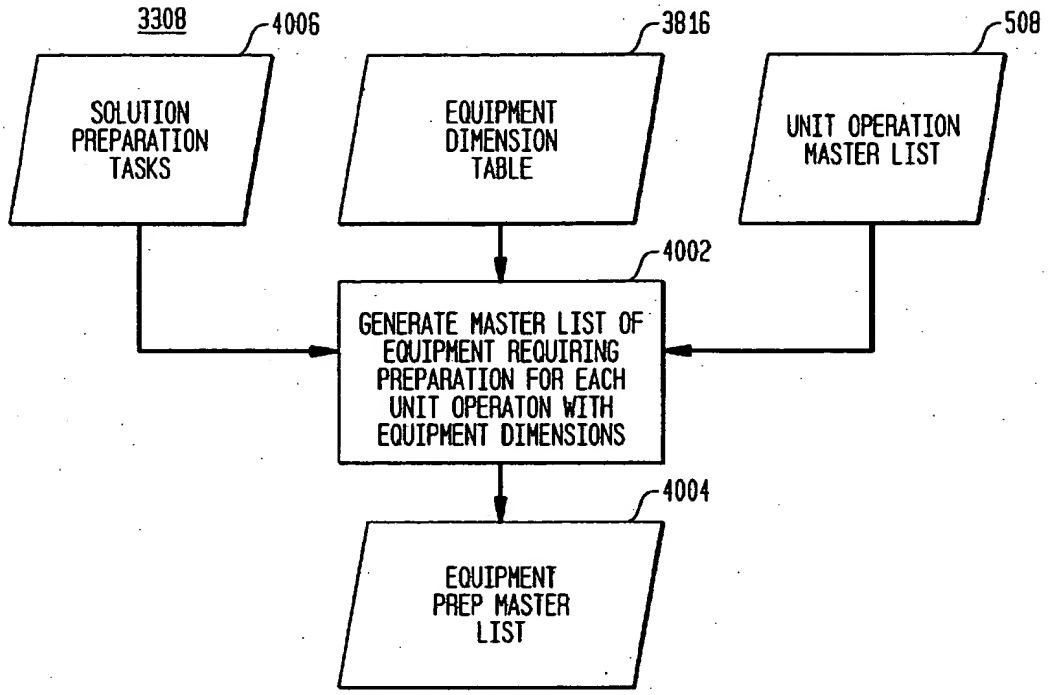
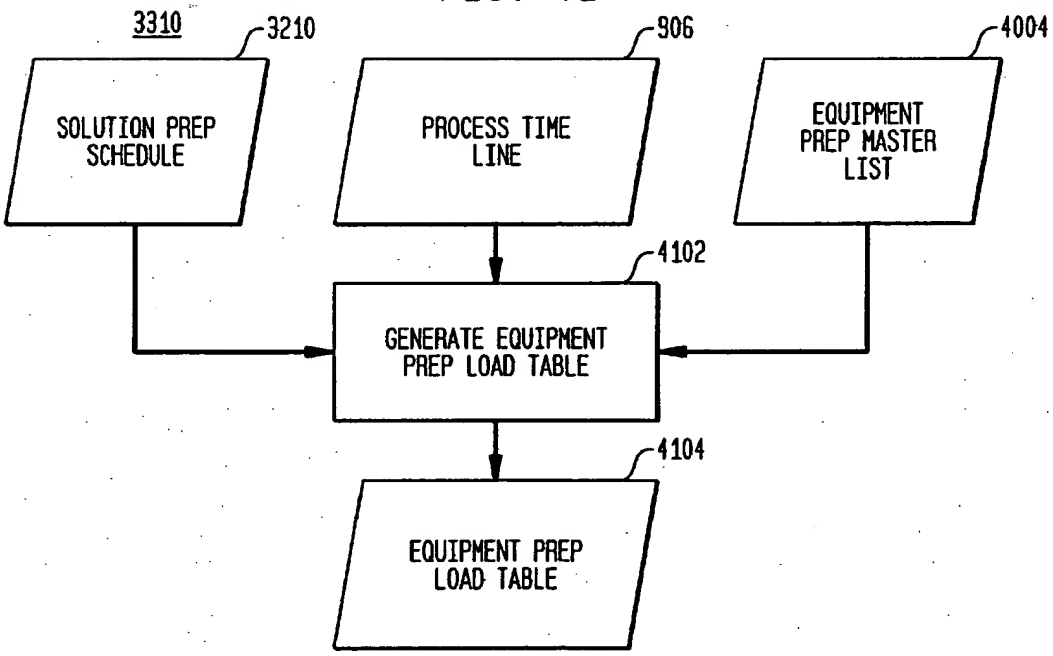


FIG. 41



Appl. No. : 09/100,088; Filed: June 19, 1998
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Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 42A-1

Equipment Prep Load Table

4202 Task	4204 Unit Oper End Time		EPC-1 Speciality Glass		4206 Total	EPC-2 Instruments	4208
	Date	Time	Siphon Tubes			PI 0.03	DO Probe 0.06
1 Inoculum Prep	06/04/96	02:30 PM			0		
2 Flask Growth	06/05/96	01:30 PM			0		
3 Seed Fermentation	06/06/96	03:30 PM			0		
4 Fermentation	06/07/96	12:00 PM			0	4 0.111	
5 Heat Exchange	06/07/96	01:00 PM			0	3	
6 Cont. Cent/Solids	06/07/96	11:51 AM			0	3 0.083	
1 Inoculum Prep	06/06/96	02:30 PM			0		
2 Flask Growth	06/07/96	01:30 PM			0		
3 Seed Fermentation	06/08/96	03:30 PM			0		
4 Fermentation	06/09/96	09:00 AM			0	4 0.111	
5 Heat Exchange	06/09/96	10:00 AM			0	3 0.083	
6 Cont. Cent/Solids	06/09/96	08:51 AM			0	3 0.083	
1 Inoculum Prep	06/08/96	02:30 PM			0		
2 Flask Growth	06/09/96	01:30 PM			0		
3 Seed Fermentation	06/10/96	03:30 PM			0		
4 Fermentation	06/03/96	10:00 AM			0	4 0.111	
5 Heat Exchange	06/11/96	09:00 AM			0	3 0.083	
6 Cont. Cent/Solids	06/11/96	08:51 AM			0	3 0.083	
7 Cell Resuspension	06/11/96	12:15 PM			0		
8 Heat Exchange	06/11/96	09:33 AM			0		
9 Cell Disruption	06/11/96	09:51 AM			0		
10 Heat Exchange	06/11/96	10:09 AM			0		

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(As Amended)

FIG. 42A-2

Equipment Prep Load Table

									EPC-3
	Fittings							Total CF	Plasticware
pH Probe 0.06	Tees 0.03	Elbows 0.02	Crosses 0.06	Reducers 0.01	Hose Barbs 0.01	Clamps 0.01			Beakers 0.03
								0.00	
								0.00	
								0.00	
	6 0.17			2 0.03	4 0.03	16 0.17		0.50	
	4 0.11				4 0.03	8 0.08		0.22	
	4 0.11				4 0.03	8 0.08		0.31	
								0.00	
								0.00	
								0.00	
	6 0.17			2 0.03	4 0.03	16 0.17		0.50	
	4 0.11				4 0.03	8 0.08		0.31	
	4 0.11				4 0.03	8 0.08		0.31	
								0.00	
								0.00	
								0.00	
	6 0.17			2 0.03	4 0.03	16 0.17		0.50	
	4 0.11				4 0.03	8 0.08		0.31	
	4 0.11				4 0.03	8 0.08		0.31	
								0.00	
								0.00	
								0.00	
								0.00	

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(As Amended)

FIG. 42B-1

4210

Equipment Items	Unit Oper End Time			Rubber Stoppers		Flexible Tubing	
	Date	Time	Flasks 0.25	Silicone 0.00	Butyl 0.03	Silicone 0.33	Neoprene 3.33
1 Inoculum Prep	06/04/96	02:30 PM					
2 Flask Growth	06/05/96	01:30 PM					
3 Seed Fermentation	06/06/96	03:30 PM		4 0.02		4 1.33	
4 Fermentation	06/07/96	12:00 PM		4 0.02		4 1.33	
5 Heat Exchange	06/07/96	01:00 PM					
6 Cont. Cent/Solids	06/07/96	11:51 AM					
1 Inoculum Prep	06/06/96	02:30 PM					
2 Flask Growth	06/07/96	01:30 PM					
3 Seed Fermentation	06/08/96	03:30 PM					
4 Fermentation	06/09/96	09:00 AM					
5 Heat Exchange	06/09/96	10:00 AM					
6 Cont. Cent/Solids	06/09/96	08:51 AM					
1 Inoculum Prep	06/08/96	02:30 PM					
2 Flask Growth	06/09/96	01:30 PM					
3 Seed Fermentation	06/10/96	03:30 PM					
4 Fermentation	06/03/96	10:00 AM					
5 Heat Exchange	06/11/96	09:00 AM					
6 Cont. Cent/Solids	06/11/96	08:51 AM					
7 Cell Resuspension	06/11/96	12:15 PM					
8 Heat Exchange	06/11/96	09:33 AM					
9 Cell Disruption	06/11/96	09:51 AM					
10 Heat Exchange	06/11/96	10:09 AM					

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(As Amended)

FIG. 42B-2

4212 4214 4216

	EPC-4			EPC-5				EPC-6			
Total CF	Small Glassware		Total CF	PP Carboys			Total CF	BSG Carboys			Total CF
	Beakers 0.03125	Flasks 0.25		10L 1.3333	20L 4.88	45L 10.7		10L 1.3333	20L 4.88	45L 10.7	
0.00		5 1.25	1.25				0.00				0.00
0.00		5 1.25	1.25				0.00				0.00
1.35		4 1.00	1				0.00				0.00
1.35			0	4 5.33			5.33				0.00
0.00			0				0.00				0.00
0.00			0				0.00				0.00
0.00		5 1.25	1.25				0.00				0.00
0.00		5 1.25	1.25				0.00				0.00
0.00			0				0.00				0.00
0.00			0				0.00				0.00
0.00			0				0.00				0.00
0.00			0				0.00				0.00
0.00		5 1.25	1.25				0.00				0.00
0.00		5 1.25	1.25				0.00				0.00
0.00			0				0.00				0.00
0.00			0				0.00				0.00
0.00			0				0.00				0.00
0.00			0				0.00				0.00
0.00			0				0.00				0.00
0.00			0				0.00				0.00
0.00		5 1.25	1.25				0.00				0.00

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For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 42C-1

Equipment Prep Load Table

Equipment Items	Unit Oper End Time		EPC-1 4218			EPC-2 4220	
			Speciality Glass		Total	Instruments	
	Date	Time	Siphon Tubes			PI 0.03	DO Probe 0.06
8 Heat Exchange	06/11/96	10:27 AM			0		
9 Cell Disruption	06/11/96	10:45 AM			0		
10 Heat Exchange	06/11/96	12:00 AM			0		
8 Heat Exchange	06/11/96	02:21 PM			0		
9 Cell Disruption	06/11/96	02:39 PM			0		
10 Heat Exchange	06/11/96	02:57 PM			0		
11 IB Resuspension	06/11/96	10:57 AM			0		
12 Centrifugation	06/11/96	11:33 AM			0		
11 IB Resuspension	06/11/96	03:06 PM			0		
12 Centrifugation	06/11/96	03:12 PM			0		
13 Renaturation	06/12/96	08:43 AM			0		
14 Buffer Exchange	06/12/96	11:47 AM			0		
15 Clarification	06/12/96	11:03 AM			0		
16 Chromatography 1	06/12/96	03:59 PM			0		
17 Chromatography 2	06/12/96	06:59 PM			0		
18 Buffer Exchange	06/12/96	08:27 PM			0		
19 Chromatography 3	06/12/96	10:07 PM			0		
20 Buffer Exchange	06/12/96	10:38 PM			0		
21 Chromatography 4	06/13/96	12:14 AM			0		
22 Sterile Filtration	06/13/96	12:48 AM			0		
Totals							

FIG. 42C-2

Equipment Prep Load Table

4220

								EPC-3
	Fittings						Total CF	Plasticware
pH Probe 0.06	Tees 0.03	Elbows 0.02	Crosses 0.06	Reducers 0.01	Hose Barbs 0.01	Clamps 0.01		Beakers 0.03
							0.00	
							0.00	
							0.00	
							0.00	
							0.00	
							0.00	
							0.00	
							0.00	
							0.00	
							0.00	
							0.00	
							0.00	
							0.00	
							0.00	
							0.00	
							0.00	
							0.00	
							0.00	
							0.00	
							0.00	
							3.25	

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FIG. 42D-1

Equipment Top Load Table 4222

Equipment Items	Unit Oper End Time			Rubber Stoppers		Flexible Tubing	
	Date	Time	Flasks 0.25	Silicone 0.00	Butyl 0.03	Silicone 0.33	Neoprene 3.33
8 Heat Exchange	06/11/96	10:27 AM					
9 Cell Disruption	06/11/96	10:45 AM					
10 Heat Exchange	06/11/96	12:00 AM					
8 Heat Exchange	06/11/96	02:21 PM					
9 Cell Disruption	06/11/96	02:39 PM					
10 Heat Exchange	06/11/96	02:57 PM					
11 IB Resuspension	06/11/96	10:57 AM					
12 Centrifugation	06/11/96	11:33 AM					
11 IB Resuspension	06/11/96	03:06 PM					
12 Centrifugation	06/11/96	03:12 PM					
13 Renaturation	06/12/96	08:43 AM					
14 Buffer Exchange	06/12/96	11:47 AM					
15 Clarification	06/12/96	11:03 AM					
16 Chromatography 1	06/12/96	03:59 PM					
17 Chromatography 2	06/12/96	06:59 PM					
18 Buffer Exchange	06/12/96	08:27 PM					
19 Chromatography 3	06/12/96	10:07 PM					
20 Buffer Exchange	06/12/96	10:38 PM					
21 Chromatography 4	06/13/96	12:14 AM					
22 Sterile Filtration	06/13/96	12:48 AM					
Totals							

FIG. 42D-2

Equipment Top Load Table

4224 4226 4228

	EPC-4			EPC-5				EPC-6			
Total CF	Small Glassware		Total CF	PP Carboys			Total CF	BSG Carboys			Total CF
	Beakers 0.03125	Flasks 0.25		10L 1.3333	20L 4.88	45L 10.7		10L 1.3333	20L 4.88	45L 10.7	
0.00			0				0.00				0.00
0.00			0				0.00				0.00
0.00		5 1.25	1.25				0.00				0.00
0.00			0				0.00				0.00
0.00			0				0.00				0.00
0.00		5 1.25	1.25				0.00				0.00
0.00			0				0.00				0.00
0.00			0				0.00				0.00
0.00			0				0.00				0.00
0.00			0				0.00				0.00
0.00			0				0.00				0.00
0.00			0				0.00				0.00
0.00			0				0.00				0.00
0.00			0				0.00				0.00
0.00			0				0.00				0.00
0.00			0				0.00				0.00
0.00			0				0.00				0.00
0.00			0				0.00				0.00
0.00			0				0.00				0.00
0.00			0				0.00				0.00
0.00			0				0.00				0.00

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FIG. 43

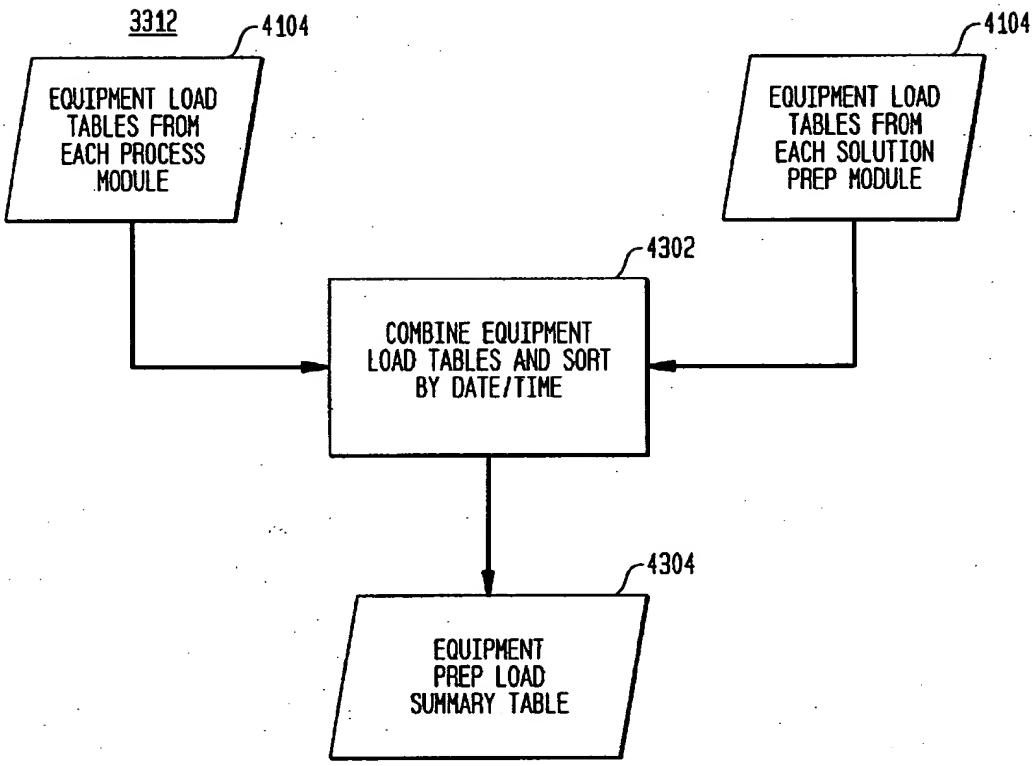
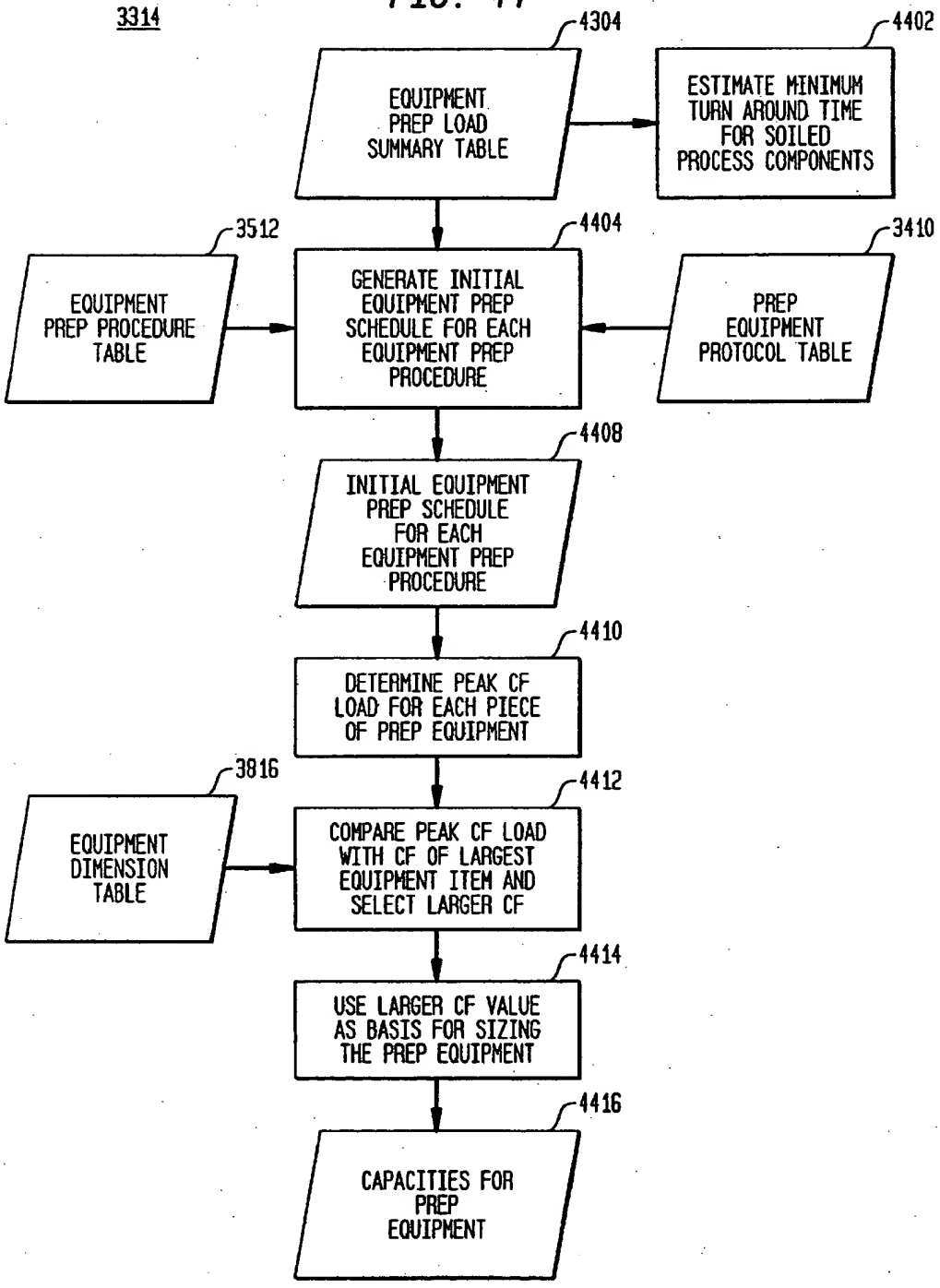


FIG. 44


3314
4304
EQUIPMENT PREP LOAD SUMMARY TABLE
4402
ESTIMATE MINIMUM TURN AROUND TIME FOR SOILED PROCESS COMPONENTS
3512
EQUIPMENT PREP PROCEDURE TABLE
4404
GENERATE INITIAL EQUIPMENT PREP SCHEDULE FOR EACH EQUIPMENT PREP PROCEDURE
3410
PREP EQUIPMENT PROTOCOL TABLE
4408
INITIAL EQUIPMENT PREP SCHEDULE FOR EACH EQUIPMENT PREP PROCEDURE
4410
DETERMINE PEAK CF LOAD FOR EACH PIECE OF PREP EQUIPMENT
3816
EQUIPMENT DIMENSION TABLE
4412
COMPARE PEAK CF LOAD WITH CF OF LARGEST EQUIPMENT ITEM AND SELECT LARGER CF
4414
USE LARGER CF VALUE AS BASIS FOR SIZING THE PREP EQUIPMENT
4416
CAPACITIES FOR PREP EQUIPMENT

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(As Amended)

FIG. 45A-1

QC Load Table-PE Module

4502 4504

	Operation	Start		Finish		QA/QC Samples Visual	
		Date	Time	Date	Time	AV-1	AV-2
		06/03/96	08:00 AM				
1	1 A Inoculum Prep						
2							
3	Set Up	06/03/96	09:30 AM	06/03/96	12:30 PM		
4	Preincubation	06/03/96	12:30 PM	06/03/96	03:30 PM		
5	Incubation	06/03/96	03:30 PM	06/04/96	02:30 PM		
6	Clean Up	06/04/96	02:30 PM	06/04/96	02:45 PM		
6	Subtotal						
7							
8	2 A Flask Growth						
9							
10	Set Up	06/04/96	12:30 PM	06/04/96	01:30 PM		
11	Preincubation	06/04/96	01:30 PM	06/04/96	02:30 PM		
12	Incubation	06/04/96	02:30 PM	06/05/96	01:30 PM		
13	Clean Up	06/05/96	01:30 PM	06/05/96	01:45 PM		
13	Subtotal						
14							
15	3 A Seed Fermentation						
16							
17	Set Up	06/05/96	11:30 AM	06/05/96	12:30 PM		
18	Preincubation	06/05/96	12:30 PM	06/05/96	01:30 PM		
19	Fermentation	06/05/96	01:30 PM	06/06/96	10:30 AM		2
20	Harvest	06/06/96	10:30 AM	06/06/96	11:00 AM		
21	CIP	06/06/96	10:30 AM	06/06/96	11:30 AM		
22	SIP	06/06/96	11:30 AM	06/06/96	12:30 PM		
23	Clean Up	06/06/96	12:30 PM	06/06/96	03:30 PM		
24	Subtotal						
25							
26	4 A Product Fermentation						
27							
28	Set Up	06/06/96	09:00 AM	06/06/96	10:00 AM		
29	Preincubation	06/06/96	10:00 AM	06/06/96	11:00 AM		
30	Fermentation	06/06/96	11:00 AM	06/07/96	08:00 AM		2
31	CIP	06/07/96	08:00 AM	06/07/96	09:00 AM		
32	SIP	06/07/96	09:00 AM	06/07/96	10:00 AM		
33	Clean Up	06/07/96	10:00 AM	06/07/96	12:00 PM		
34	Subtotal						
35							
36	5 A Heat Exchange						
37							
38	Set Up	06/07/96	08:00 AM	06/07/96	08:30 AM		
39	Transfer	06/07/96	08:00 AM	06/07/96	09:00 AM		
40	CIP	06/07/96	09:00 AM	06/07/96	10:00 AM		
41	SIP	06/07/96	10:00 AM	06/07/96	11:00 AM		
42	Clean Up	06/07/96	11:00 AM	06/07/96	01:00 PM		
43	Subtotal						
44							
45	6 A Cont. Cent./Solids						
46							
47	Set Up	06/07/96	08:00 AM	06/07/96	09:00 AM		

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(As Amended)

FIG. 45A-2

QC Load Table-PE Module

4506

Chemical						Biochemical							Immulogical		Act.
AC-1	AC-2	AC-3	AC-4	AC-5	AC-6	AB-1	AB-2	AB-3	AB-4	AB-5	AB-6	AB-7	AI-1	AI-2	AA-1
								3					3		

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(As Amended)

FIG. 45B-1

QC Load Table-PE Module

	Operation	Start		Finish		QA/QC Samples Visual	
		Date	Time	Date	Time	AV-1	AV-2
		06/03/96	08:00 AM				
48	Centrifugation	06/07/96	09:00 AM	06/07/96	10:00 AM		
49	Wash	06/07/96	10:00 AM	06/07/96	10:06 AM		
50	CIP	06/07/96	10:06 AM	06/07/96	10:21 AM		
51	SIP	06/07/96	10:21 AM	06/07/96	11:21 AM		
52	Clean Up	06/07/96	11:21 AM	06/07/96	11:51 AM		
53	Subtotal						
54							
55	1 B Inoculum Prep						
56							
57	Set Up	06/03/96	01:30 PM	06/03/96	02:30 PM		
58	Preincubation	06/03/96	02:30 PM	06/03/96	03:30 PM		
59	Incubation	06/03/96	03:30 PM	06/04/96	02:30 PM		
60	Clean Up	06/04/96	02:30 PM	06/04/96	02:45 PM		
60	Subtotal						
61							
62	2 B Flask Growth						
63							
64	Set Up	06/04/96	12:30 PM	06/04/96	01:30 PM		
65	Preincubation	06/04/96	01:30 PM	06/04/96	02:30 PM		
66	Incubation	06/04/96	02:30 PM	06/05/96	01:30 PM		
67	Clean Up	06/05/96	01:30 PM	06/05/96	01:45 PM		
67	Subtotal						
68							
69	3 B Seed Fermentation						
70							
71	Set Up	06/05/96	11:30 AM	06/05/96	12:30 PM		
72	Preincubation	06/05/96	12:30 PM	06/05/96	01:30 PM		
73	Fermentation	06/05/96	01:30 PM	06/06/96	10:30 AM		
74	Harvest	06/06/96	10:30 AM	06/06/96	11:00 AM		2
75	CIP	06/06/96	10:30 AM	06/06/96	11:30 AM		
76	SIP	06/06/96	11:30 AM	06/06/96	12:30 PM		
77	Clean Up	06/06/96	12:30 PM	06/06/96	03:30 PM		
78	Subtotal						
79							
80	4 B Product Fermentation						
81							
82	Set Up	06/06/96	09:00 AM	06/06/96	10:00 AM		
83	Preincubation	06/06/96	10:00 AM	06/06/96	11:00 AM		
84	Fermentation	06/06/96	11:00 AM	06/07/96	08:00 AM		
85	CIP	06/07/96	08:00 AM	06/07/96	09:00 AM		2
86	SIP	06/07/96	09:00 AM	06/07/96	10:00 AM		
87	Clean Up	06/07/96	10:00 AM	06/07/96	12:00 AM		
88	Subtotal						
89							
90	5 B Heat Exchange						
91							
92	Set Up	06/07/96	08:00 AM	06/07/96	08:30 AM		
93	Transfer	06/07/96	08:00 AM	06/07/96	09:00 AM		
94	CIP	06/07/96	09:00 AM	06/07/96	10:00 AM		

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Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 45B-2

QC Load Table-PE Module

4506

Chemical						Biochemical							Immulogical		Act.
AC-1	AC-2	AC-3	AC-4	AC-5	AC-6	AB-1	AB-2	AB-3	AB-4	AB-5	AB-6	AB-7	AI-1	AI-2	AA-1
								3		3			3		
								3					3		

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Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 45C-1

QC Load Table-PE Module

	Operation	Start		Finish		QA/QC Samples Visual	
		Date	Time	Date	Time	AV-1	AV-2
		06/03/96	08:00 AM				
95	SIP	06/07/96	10:00 AM	06/07/96	11:00 AM		
96	Clean Up	06/07/96	11:00 AM	06/07/96	01:00 AM		
97	Subtotal						
98							
99	6 B Cont. Cent/Solilds						
100							
101	Set Up	06/07/96	08:00 AM	06/07/96	09:00 AM		
102	Centrifugation	06/07/96	09:00 AM	06/07/96	10:00 AM		
103	Wash	06/07/96	10:00 AM	06/07/96	10:06 AM		
104	CIP	06/07/96	10:06 AM	06/07/96	10:21 AM		
105	SIP	06/07/96	10:21 AM	06/07/96	11:21 AM		
106	Clean Up	06/07/96	11:21 AM	06/07/96	11:51 AM		
107	Subtotal						
108							
109	1 C Inoculum Prep						
110							
111	Set Up	06/03/96	01:30 PM	06/03/96	02:30 PM		
112	Preincubation	06/03/96	02:30 PM	06/03/96	03:30 PM		
113	Incubation	06/03/96	03:30 PM	06/04/96	02:30 PM		
114	Clean Up	06/04/96	02:30 PM	06/04/96	02:45 PM		
114	Subtotal						
115							
116	2 C Flask Growth						
117							
118	Set Up	06/04/96	12:30 PM	06/04/96	01:30 PM		
119	Preincubation	06/04/96	01:30 PM	06/04/96	02:30 PM		
120	Incubation	06/04/96	02:30 PM	06/05/96	01:30 PM		
121	Clean Up	06/05/96	01:30 PM	06/05/96	01:45 PM		
121	Subtotal						
122							
123	3 C Seed Fermentation						
124							
125	Set Up	06/05/96	11:30 AM	06/05/96	12:30 PM		
126	Preincubation	06/05/96	12:30 PM	06/05/96	01:30 PM		
127	Fermentation	06/05/96	01:30 PM	06/06/96	10:30 AM		
128	Harvest	06/06/96	10:30 AM	06/06/96	11:00 AM		2
129	CIP	06/06/96	10:30 AM	06/06/96	11:30 AM		
130	SIP	06/06/96	11:30 AM	06/06/96	12:30 PM		
131	Clean Up	06/06/96	12:30 PM	06/06/96	03:30 PM		
132	Subtotal						
133							
134	4 C Product Fermentation						
135							
136	Set Up	06/06/96	09:00 AM	06/06/96	10:00 AM		
137	Preincubation	06/06/96	10:00 AM	06/06/96	11:00 AM		
138	Fermentation	06/06/96	11:00 AM	06/07/96	08:00 AM		
139	CIP	06/07/96	08:00 AM	06/07/96	09:00 AM		2
140	SIP	06/07/96	09:00 AM	06/07/96	10:00 AM		
141	Clean Up	06/07/96	10:00 AM	06/07/96	12:00 PM		

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(As Amended)

FIG. 45C-2

QC Load Table-PE Module

Chemical						Biochemical							Immulogical		Act.
AC-1	AC-2	AC-3	AC-4	AC-5	AC-6	AB-1	AB-2	AB-3	AB-4	AB-5	AB-6	AB-7	AI-1	AI-2	AA-1
								3		3			3		
								3					3		

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(As Amended)

FIG. 45D-1

QC LOAD TABLE-PE MODULE

	Operation	Start		Finish		QA/QC Samples Visual	
		Date	Time	Date	Time	AV-1	AV-2
		06/03/96	08:00 AM				
142	Subtotal						
143							
144	5 C Heat Exchange						
145							
146	Set Up	06/07/96	08:00 AM	06/07/96	08:30 AM		
147	Transfer	06/07/96	08:00 AM	06/07/96	09:00 AM		
148	CIP	06/07/96	09:00 AM	06/07/96	10:00 AM		
149	SIP	06/07/96	10:00 AM	06/07/96	11:00 AM		
150	Clean Up	06/07/96	11:00 AM	06/07/96	01:00 PM		
151	Subtotal						
152							
153	6 C Cont. Cent./Solids						
154							
155	Set Up	06/07/96	08:00 AM	06/07/96	09:00 AM		
156	Centrifugation	06/07/96	09:00 AM	06/07/96	10:00 AM		
157	Wash	06/07/96	10:00 AM	06/07/96	10:06 AM		
158	CIP	06/07/96	10:06 AM	06/07/96	10:21 AM		
159	SIP	06/07/96	10:21 AM	06/07/96	11:21 AM		
160	Clean Up	06/07/96	11:21 AM	06/07/96	11:51 AM		
161	Subtotal						
162							
163	7 A Resolubilization						
164							
165	Set Up	06/07/96	09:06 AM	06/07/96	10:06 AM		
166	Dilution	06/07/96	10:06 AM	06/07/96	10:36 AM		
167	Agitate	06/07/96	10:36 AM	06/07/96	11:36 AM		
168	CIP	06/07/96	11:36 AM	06/07/96	12:36 PM		
169	SIP	06/07/96	12:36 PM	06/07/96	01:36 PM		
170	Clean Up	06/07/96	01:36 PM	06/07/96	02:36 PM		
171	Subtotal						
172							
173	8 A Heat Exchange						
174							
175	Set Up	06/07/96	11:06 AM	06/07/96	11:36 AM		
176	Transfer	06/07/96	11:36 AM	06/07/96	11:54 AM		
177	CIP	06/07/96	11:54 AM	06/07/96	11:54 AM		
178	SIP	06/07/96	11:54 AM	06/07/96	11:54 AM		
179	Clean Up	06/07/96	11:54 AM	06/07/96	11:54 AM		
180	Subtotal						
181							
182	9 A Hommogenization						
183							
184	Set Up	06/07/96	11:39 AM	06/07/96	11:54 AM		
185	Lysis	06/07/96	11:54 AM	06/07/96	12:34 PM		
186	CIP	06/07/96	12:34 PM	06/07/96	12:34 PM		
187	SIP	06/07/96	12:34 PM	06/07/96	12:34 PM		
188	Clean Up	06/07/96	12:34 PM	06/07/96	12:34 PM		
189	Subtotal						
190							

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(As Amended)

FIG. 45D-2

QC LOAD TABLE-PE MODULE

Chemical						Biochemical							Immulogical		Act.
AC-1	AC-2	AC-3	AC-4	AC-5	AC-6	AB-1	AB-2	AB-3	AB-4	AB-5	AB-6	AB-7	AI-1	AI-2	AA-1
								3		3			3		

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(As Amended)

FIG. 45E-1

QC LOAD TABLE-PE MODULE

	Operation	Start		Finish		QA/QC Samples Visual	
		Date	Time	Date	Time	AV-1	AV-2
		06/03/96	08:00 AM				
191	10 A Heat Exchange						
192							
193	Set Up	06/07/96	12:04 PM	06/07/96	12:34 PM		
194	Transfer	06/07/96	12:34 PM	06/07/96	12:52 PM		
195	CIP	06/07/96	12:52 PM	06/07/96	12:52 PM		
196	SIP	06/07/96	12:52 PM	06/07/96	12:52 PM		
197	Clean Up	06/07/96	12:52 PM	06/07/96	12:52 PM		
198	Subtotal						
199							
200	8 B Heat Exchange						
201							
202	Set Up	06/07/96	12:52 PM	06/07/96	12:52 PM		
203	Transfer	06/07/96	12:52 PM	06/07/96	01:10 PM		
204	CIP	06/07/96	01:10 PM	06/07/96	01:10 PM		
205	SIP	06/07/96	01:10 PM	06/07/96	01:10 PM		
206	Clean Up	06/07/96	01:10 PM	06/07/96	01:10 PM		
207	Subtotal						
208							
209	9 B Hommogenization						
210							
211	Set Up	06/07/96	01:10 PM	06/07/96	01:10 PM		
212	Lysis	06/07/96	01:10 PM	06/07/96	01:51 PM		
213	CIP	06/07/96	01:51 PM	06/07/96	01:51 PM		
214	SIP	06/07/96	01:51 PM	06/07/96	01:51 PM		
215	Clean Up	06/07/96	01:51 PM	06/07/96	01:51 PM		
216	Subtotal						
217							
218	10 B Heat Exchange						
219							
220	Set Up	06/07/96	01:21 PM	06/07/96	01:51 PM		
221	Transfer	06/07/96	01:51 PM	06/07/96	02:09 PM		
222	CIP	06/07/96	02:09 PM	06/07/96	02:09 PM		
223	SIP	06/07/96	02:09 PM	06/07/96	02:09 PM		
224	Clean Up	06/07/96	02:09 PM	06/07/96	02:09 PM		
225	Subtotal						
226							
227	8 C Heat Exchange						
228							
229	Set Up	06/07/96	02:09 PM	06/07/96	02:09 PM		
230	Transfer	06/07/96	02:09 PM	06/07/96	02:27 PM		
231	CIP	06/07/96	02:27 PM	06/07/96	03:27 PM		
232	SIP	06/07/96	03:27 PM	06/07/96	04:27 PM		
233	Clean Up	06/07/96	04:27 PM	06/07/96	05:27 PM		
234	Subtotal						
235							
236	9 C Hommogenization						
237							
238	Set Up	06/07/96	02:27 PM	06/07/96	02:27 PM		
239	Lysis	06/07/96	02:27 PM	06/07/96	03:07 PM		

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FIG. 45E-2

QC LOAD TABLE-PE MODULE

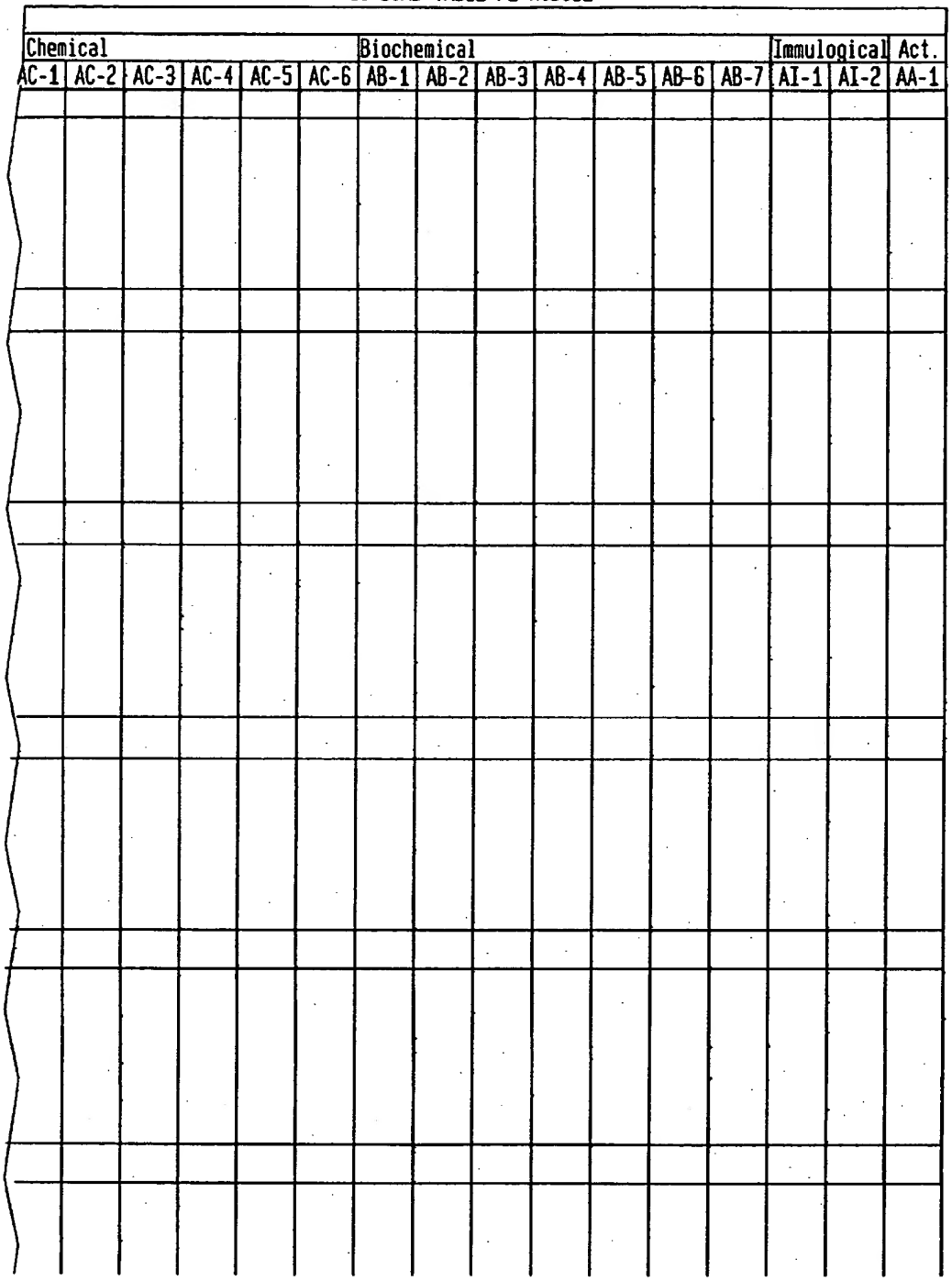

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FIG. 45F-1

QC LOAD TABLE-PE MODULE

	Operation	Start		Finish		QA/QC Samples Visual	
		Date	Time	Date	Time	AV-1	AV-2
		06/03/96	08:00 AM				
240	CIP	06/07/96	03:07 PM	06/07/96	04:07 PM		
241	SIP	06/07/96	04:07 PM	06/07/96	05:07 PM		
242	Clean Up	06/07/96	05:07 PM	06/07/96	06:07 PM		
243	Subtotal						
244							
245	10 C Heat Exchange						
246							
247	Set Up	06/07/96	03:07 PM	06/07/96	03:07 PM		
248	Transfer	06/07/96	03:07 PM	06/07/96	03:25 PM		
249	CIP	06/07/96	03:25 PM	06/07/96	04:25 PM		
250	SIP	06/07/96	04:25 PM	06/07/96	05:25 PM		
251	Clean Up	06/07/96	05:25 PM	06/07/96	06:25 PM		
252	Subtotal						
253							
254	11 A Resolubilization						
255							
256	Set Up	06/07/96	11:52 AM	06/07/96	12:52 PM		
257	Dilution	06/07/96	12:52 PM	06/07/96	01:22 PM		
258	Agitate	06/07/96	01:22 PM	06/07/96	01:52 PM		
259	CIP	06/07/96	01:52 PM	06/07/96	01:52 PM		
260	SIP	06/07/96	01:52 PM	06/07/96	01:52 PM		
261	Clean Up	06/07/96	01:52 PM	06/07/96	01:52 PM		
262	Subtotal						
263							
264	12 A Cont.Cent/Solids						
265							
266	Set Up	06/07/96	12:52 PM	06/07/96	01:52 PM		
267	Centrifugation	06/07/96	01:52 PM	06/07/96	02:22 PM		
268	Wash	06/07/96	02:22 PM	06/07/96	02:28 PM		
269	CIP	06/07/96	02:28 PM	06/07/96	02:28 PM		
270	SIP	06/07/96	02:28 PM	06/07/96	02:28 PM		
271	Clean Up	06/07/96	02:28 PM	06/07/96	02:28 PM		
272	Subtotal						
273							
274	11 B Resolubilization						
275							
276	Set Up	06/07/96	02:28 PM	06/07/96	02:28 PM		
277	Dilution	06/07/96	02:28 PM	06/07/96	02:58 PM		
278	Agitate	06/07/96	02:58 PM	06/07/96	03:13 PM		
279	CIP	06/07/96	03:13 PM	06/07/96	04:13 PM		
280	SIP	06/07/96	04:13 PM	06/07/96	05:13 PM		
281	Clean Up	06/07/96	05:13 PM	06/07/96	06:13 PM		
282	Subtotal						
283							
284	12 B Cont.Cent/Solids						
285							
286	Set Up	06/07/96	02:13 PM	06/07/96	03:13 PM		
287	Centrifugation	06/07/96	03:13 PM	06/07/96	03:43 PM		
288	Wash	06/07/96	03:43 PM	06/07/96	03:49 PM		

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(As Amended)

FIG. 45F-2

QC LOAD TABLE-PE MODULE

Chemical													Immulogical		Act.
AC-1	AC-2	AC-3	AC-4	AC-5	AC-6	AB-1	AB-2	AB-3	AB-4	AB-5	AB-6	AB-7	AI-1	AI-2	AA-1

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FIG. 45G-1

QC LOAD TABLE-PE MODULE

	Operation			Finish		QA/QC Samples Visual	
		Date	Time	Date	Time	AV-1	AV-2
		06/03/96	08:00 AM				
289	CIP	06/07/96	03:49 PM	06/07/96	04:04 PM		
290	SIP	06/07/96	04:04 PM	06/07/96	05:04 PM		
291	Clean Up	06/07/96	05:04 PM	06/07/96	05:34 PM		
292	Subtotal						
293							
294	13 A Resolubilization						
295							
296	Set Up	06/07/96	01:28 PM	06/07/96	02:28 PM		
297	Dilution	06/07/96	02:28 PM	06/07/96	02:58 PM		
298	Agitate	06/07/96	02:58 PM	06/08/96	08:58 AM		
299	CIP	06/08/96	08:58 AM	06/08/96	09:58 AM		
300	SIP	06/08/96	09:58 AM	06/08/96	10:58 AM		
301	Clean Up	06/08/96	10:58 AM	06/08/96	11:58 AM		
302	Subtotal						
303							
304	14 A Concentration						
305							
306	Set Up	06/08/96	06:38 AM	06/08/96	07:38 AM		
307	Flush	06/08/96	07:38 AM	06/08/96	08:18 AM		
308	Prime	06/08/96	08:18 AM	06/08/96	08:58 AM		
309	Concentration	06/08/96	08:58 AM	06/08/96	09:58 AM		
310	Dilution	06/08/96	09:58 AM	06/08/96	10:25 AM		
311	Wash	06/08/96	10:25 AM	06/08/96	11:19 AM		
312	Flush	06/08/96	11:19 AM	06/08/96	11:39 AM		
313	Store	06/08/96	11:39 AM	06/08/96	12:19 PM		
314	CIP	06/08/96	12:19 PM	06/08/96	01:19 PM		
315	SIP	06/08/96	01:19 PM	06/08/96	02:19 PM		
316	Clean Up	06/08/96	02:19 PM	06/08/96	03:19 PM		
317	Subtotal						
318							
319	15 A Microfiltration						
320							
321	Set Up	06/08/96	10:03 AM	06/08/96	11:03 AM		
322	Flush	06/08/96	11:03 AM	06/08/96	11:11 AM		
323	Prime	06/08/96	11:11 AM	06/08/96	11:19 AM		
324	Filtration	06/08/96	11:19 AM	06/08/96	11:49 AM		
325	Wash	06/08/96	11:49 AM	06/08/96	11:49 AM		
326	Regenerate	06/08/96	11:49 AM	06/08/96	11:51 AM		
327	Store	06/08/96	11:51 AM	06/08/96	11:55 AM		
328	CIP	06/08/96	11:55 AM	06/08/96	12:55 PM		
329	SIP	06/08/96	12:55 PM	06/08/96	01:55 PM		
330	Clean Up	06/08/96	01:55 PM	06/08/96	02:55 PM		
331	Subtotal						
332							
333	16 A P/A MPLC						
334							
335	Equilibration	06/08/96	10:17 AM	06/08/96	11:24 AM		
336	Load	06/08/96	11:49 AM	06/08/96	12:31 PM		
337	Wash	06/08/96	12:31 PM	06/08/96	01:52 PM		

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(As Amended)

FIG. 45G-2

QC LOAD TABLE-PE MODULE

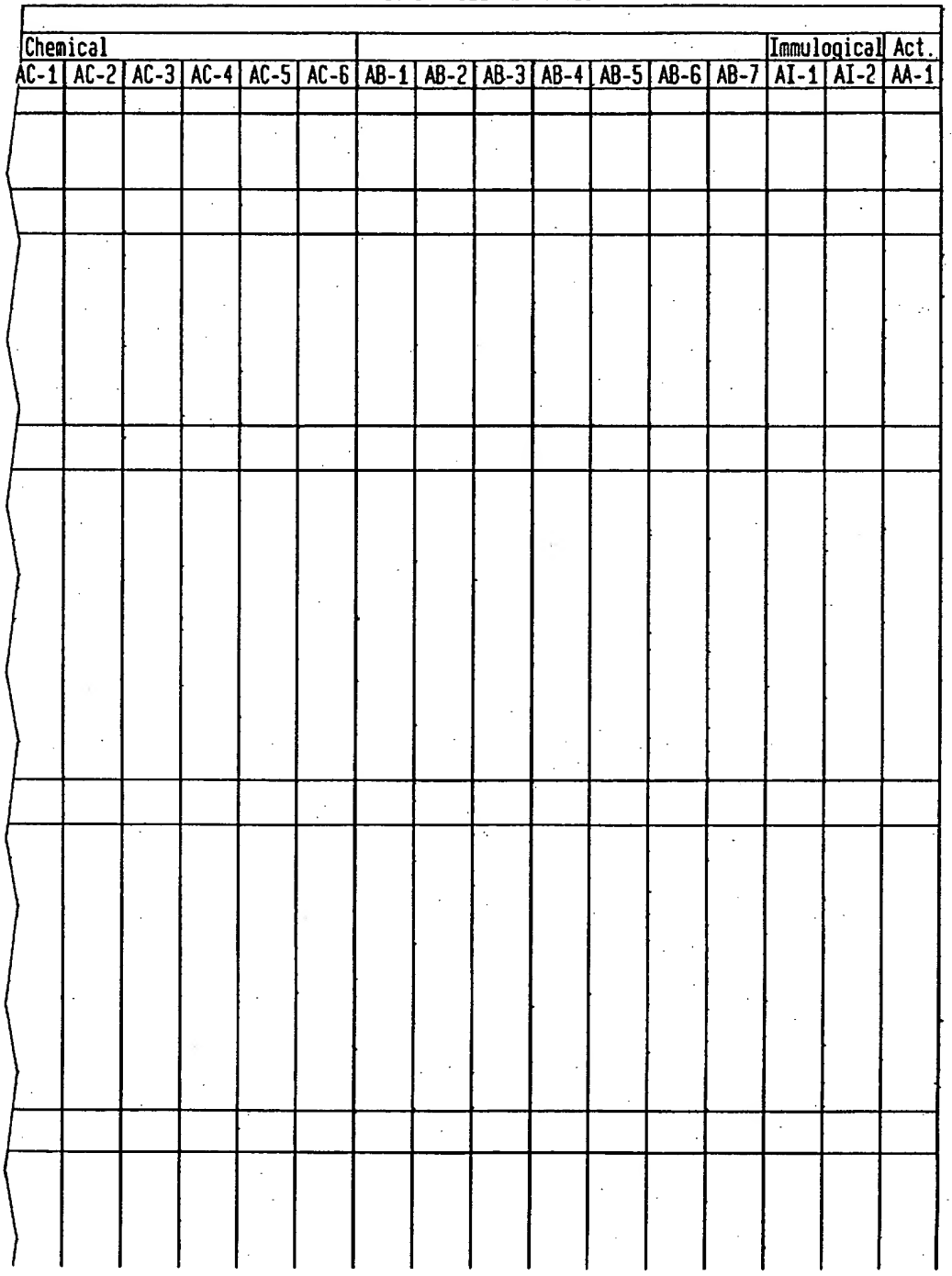

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FIG. 45H-1

QC LOAD TABLE-PE MODULE

	Operation			Finish		QA/QC Samples Visual	
		Date	Time	Date	Time	AV-1	AV-2
		06/03/96	08:00 AM				
338	Elute A	06/08/96	01:52 PM	06/08/96	03:12 PM		
339	Elute B	06/08/96	03:12 PM	06/08/96	03:12 PM		
340	Regenerate	06/08/96	03:12 PM	06/08/96	03:25 PM		
341	Store	06/08/96	03:25 PM	06/08/96	03:52 PM		
342	CIP	06/08/96	03:52 PM	06/08/96	04:52 PM		
343	SIP	06/08/96	04:52 PM	06/08/96	05:52 PM		
344	Clean Up	06/08/96	05:52 PM	06/08/96	06:52 PM		
345	Subtotal						
346							
347							
348	17 A P/A MPLC						
349							
350	Equilibration	06/08/96	02:59 PM	06/08/96	03:38 PM		
351	Load	06/08/96	03:12 PM	06/08/96	04:17 PM		
352	Wash	06/08/96	04:17 PM	06/08/96	05:03 PM		
353	Elute A	06/08/96	05:03 PM	06/08/96	05:49 PM		
354	Elute B	06/08/96	05:49 PM	06/08/96	05:49 PM		
355	Regenerate	06/08/96	05:49 PM	06/08/96	05:57 PM		
356	Store	06/08/96	05:57 PM	06/08/96	06:13 PM		
357	CIP	06/08/96	06:13 PM	06/08/96	07:13 PM		
358	SIP	06/08/96	07:13 PM	06/08/96	08:13 PM		
359	Clean Up	06/08/96	08:13 PM	06/08/96	09:13 PM		
360	Subtotal						
361							
362	18 A Flow Dialysis						
363							
364	Set Up	06/08/96	03:29 PM	06/08/96	04:29 PM		
365	Flush	06/08/96	04:29 PM	06/08/96	05:09 PM		
366	Prime	06/08/96	05:09 PM	06/08/96	05:49 PM		
367	Dialysis	06/08/96	05:49 PM	06/08/96	06:49 PM		
368	Wash	06/08/96	06:49 PM	06/08/96	06:49 PM		
369	Flush	06/08/96	06:49 PM	06/08/96	07:09 PM		
370	Store	06/08/96	07:09 PM	06/08/96	07:49 PM		
371	CIP	06/08/96	07:49 PM	06/08/96	08:49 PM		
372	SIP	06/08/96	08:49 PM	06/08/96	09:49 PM		
373	Clean Up	06/08/96	09:49 PM	06/08/96	10:49 PM		
374	Subtotal						
375							
376	19 A P/A MPLC						
377							
378	Equilibration	06/08/96	05:59 PM	06/08/96	06:31 PM		
379	Load	06/08/96	06:49 PM	06/08/96	07:03 PM		
380	Wash	06/08/96	07:03 PM	06/08/96	07:41 PM		
381	Elute A	06/08/96	07:41 PM	06/08/96	08:20 PM		
382	Elute B	06/08/96	08:20 PM	06/08/96	08:20 PM		
383	Regenerate	06/08/96	08:20 PM	06/08/96	08:26 PM		
384	Store	06/08/96	08:26 PM	06/08/96	08:39 PM		
385	CIP	06/08/96	08:39 PM	06/08/96	09:39 PM		
386	SIP	06/08/96	09:39 PM	06/08/96	10:39 PM		

Appl. No. : 09/100,088; Filed: June 19, 1998
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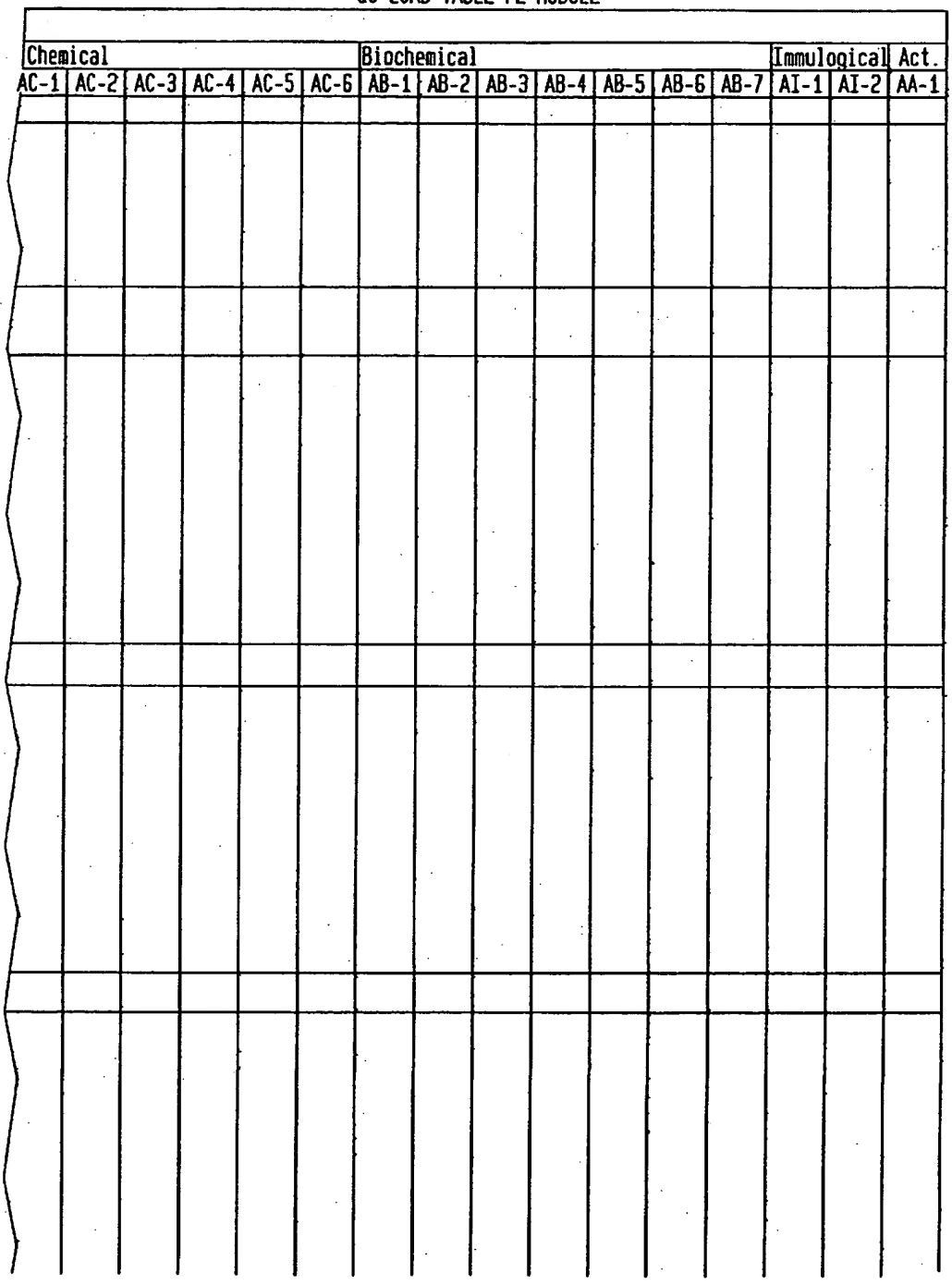
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 45H-2

QC LOAD TABLE-PE MODULE



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For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
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FIG. 45I-1
QC LOAD TABLE-PE MODULE

	Operation			Finish		QA/QC Samples Visual		
		Date	Time	Date	Time	AV-1	AV-2	
		06/03/96	08:00 AM					
387	Clean Up	06/08/96	10:39 PM	06/08/96	11:39 PM			
388	Subtotal							
389								
390	20 A Flow Dialysis							
391								
392	Set Up	06/08/96	07:00 PM	06/08/96	07:00 PM			
393	Flush	06/08/96	07:00 PM	06/08/96	07:40 PM			
394	Prime	06/08/96	07:40 PM	06/08/96	08:20 PM			
395	Dialysis	06/08/96	08:20 PM	06/08/96	10:20 PM			
396	Wash	06/08/96	10:20 PM	06/08/96	10:20 PM			
397	Flush	06/08/96	10:20 PM	06/08/96	10:40 PM			
398	Store	06/08/96	10:40 PM	06/08/96	11:20 PM			
399	CIP	06/08/96	11:20 PM	06/08/96	11:20 PM			
400	SIP	06/08/96	11:20 PM	06/08/96	11:20 PM			
401	Clean Up	06/08/96	11:20 PM	06/09/96	12:20 AM			
402	Subtotal							
403								
404	21 A P/A MPLC							
405								
406	Equilibration	06/08/96	09:28 PM	06/08/96	09:57 PM			
407	Load	06/08/96	10:20 PM	06/08/96	10:26 PM			
408	Wash	06/08/96	10:26 PM	06/08/96	11:01 PM			
409	Elute A	06/08/96	11:01 PM	06/08/96	11:36 PM			
410	Elute B	06/08/96	11:36 PM	06/08/96	11:36 PM			
411	Regenerate	06/08/96	11:36 PM	06/08/96	11:42 PM			
412	Store	06/08/96	11:42 PM	06/08/96	11:54 PM			
413	CIP	06/08/96	11:54 PM	06/08/96	11:54 PM			
414	SIP	06/08/96	11:54 PM	06/08/96	11:54 PM			
415	Clean Up	06/08/96	11:54 PM	06/09/96	12:54 AM			
416	Subtotal							
417								
418	22 A Sterile Filtration							
419								
420	Set Up	06/09/96	08:06 AM	06/09/96	08:36 AM			
421	Filtration	06/08/96	11:36 PM	06/09/96	12:06 AM			
422	Storage	06/09/96	12:06 AM	06/09/96	12:36 AM			
423	CIP	06/09/96	12:36 AM	06/09/96	12:36 AM			
424	SIP	06/09/96	12:36 AM	06/09/96	12:36 AM			
425	Clean Up	06/09/96	12:36 AM	06/09/96	01:36 AM			
426	Subtotal							

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(As Amended)

FIG. 45I-2
QC LOAD TABLE-PE MODULE

Chemical						Biochemical							Immulogical		Act.
AC-1	AC-2	AC-3	AC-4	AC-5	AC-6	AB-1	AB-2	AB-3	AB-4	AB-5	AB-6	AB-7	AI-1	AI-2	AA-1

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(As Amended)

3316

FIG. 46

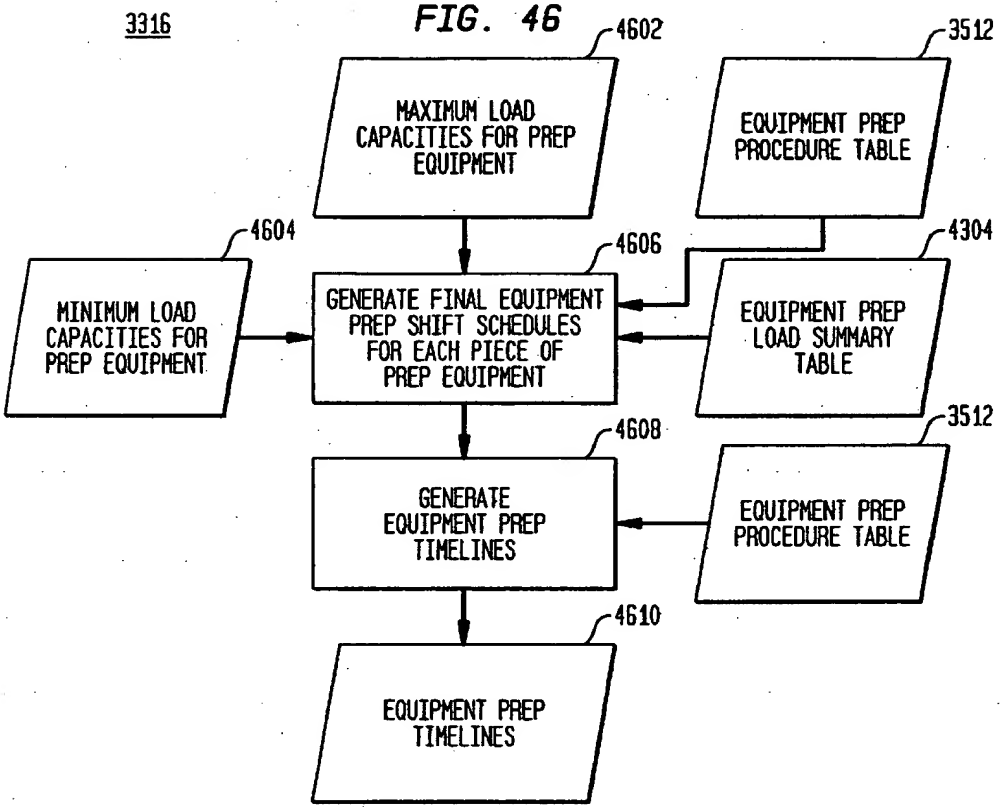
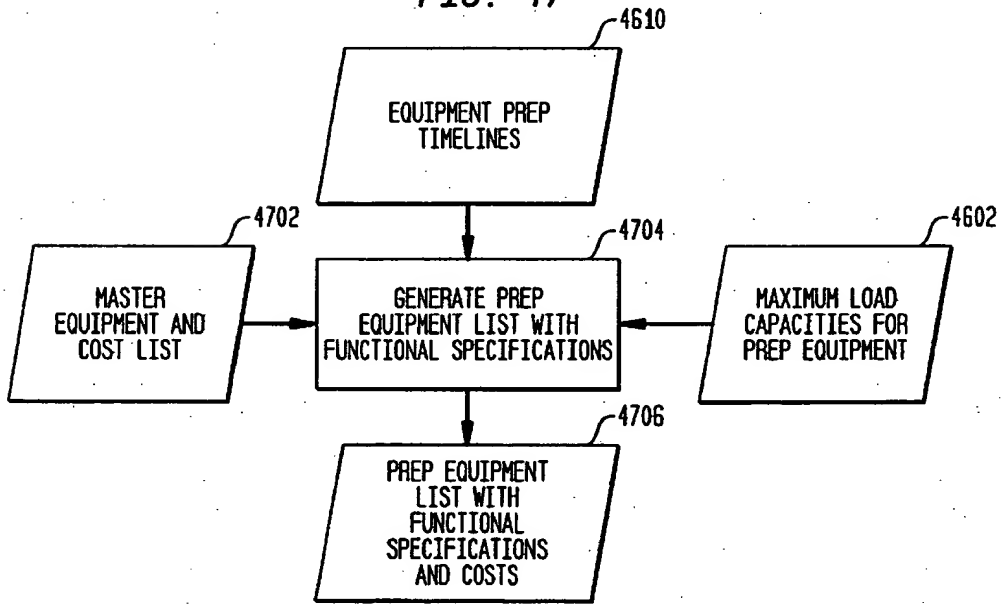


FIG. 47



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Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 48

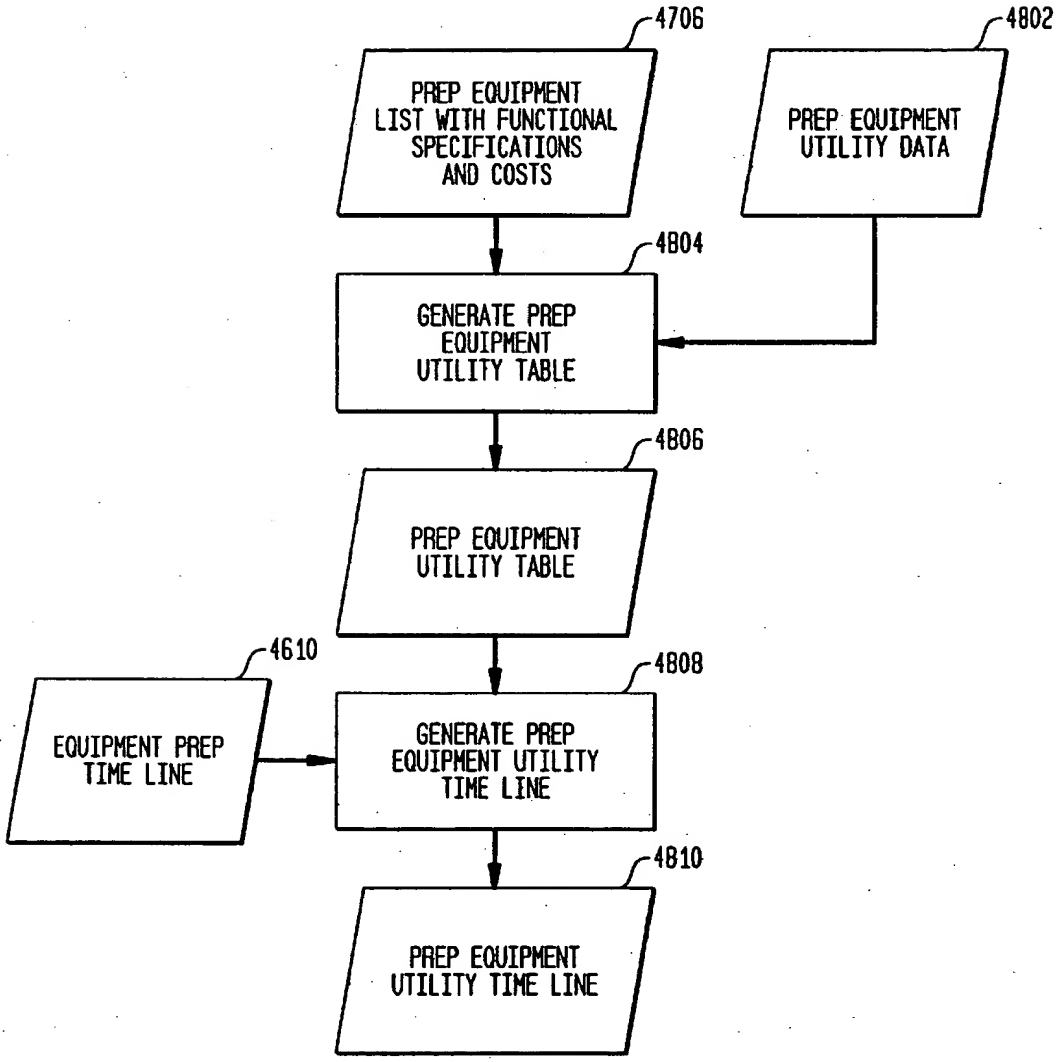


FIG. 49

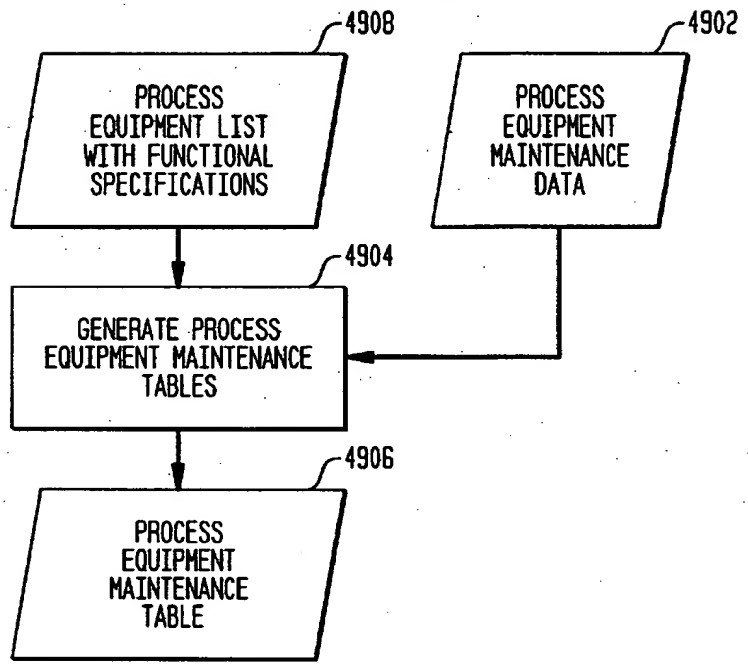
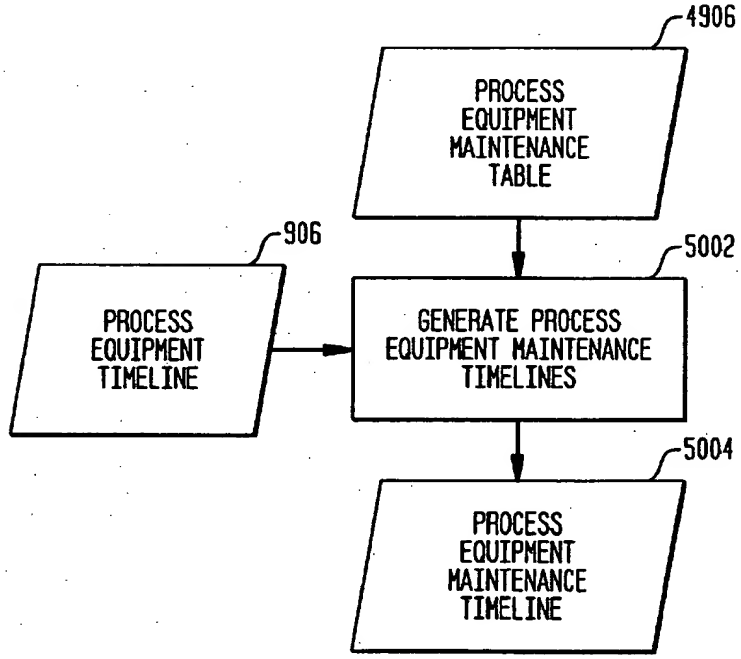

4908
PROCESS EQUIPMENT LIST WITH FUNCTIONAL SPECIFICATIONS
4902
PROCESS EQUIPMENT MAINTENANCE DATA
4904
GENERATE PROCESS EQUIPMENT MAINTENANCE TABLES
4906
PROCESS EQUIPMENT MAINTENANCE TABLE

FIG. 50


4906
PROCESS EQUIPMENT MAINTENANCE TABLE
906
PROCESS EQUIPMENT TIMELINE
5002
GENERATE PROCESS EQUIPMENT MAINTENANCE TIMELINES
5004
PROCESS EQUIPMENT MAINTENANCE TIMELINE

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For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 51

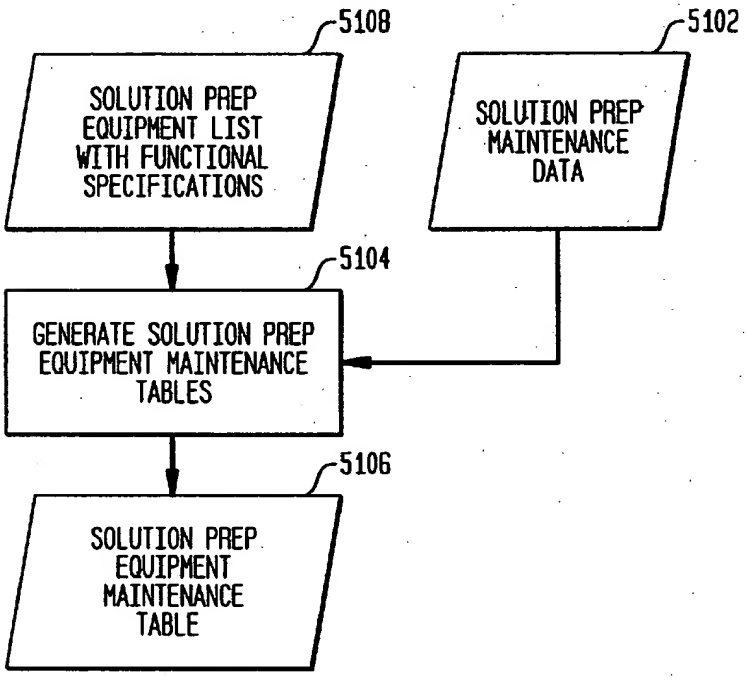
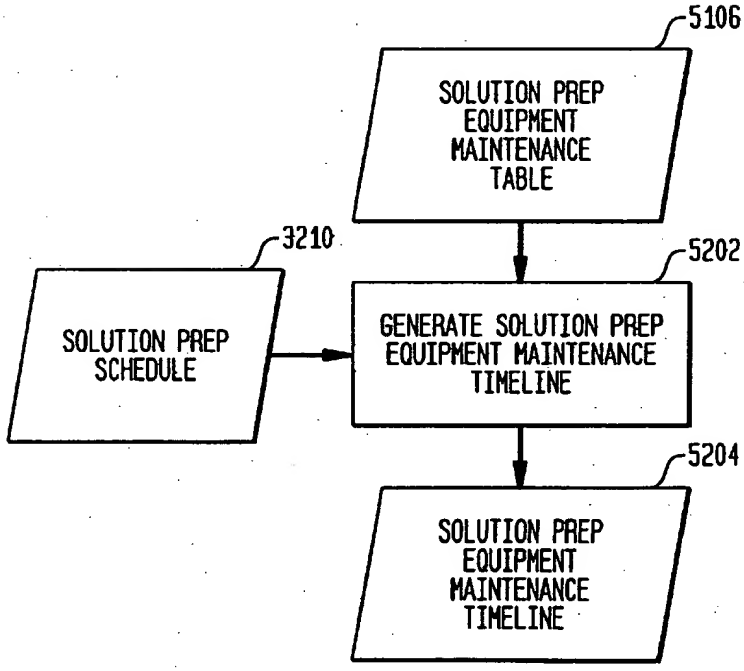


FIG. 52



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For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 53

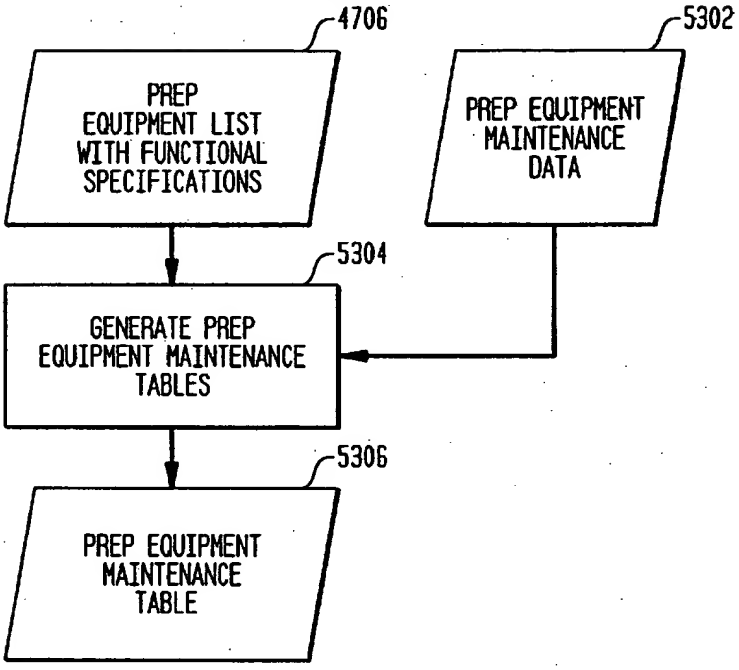
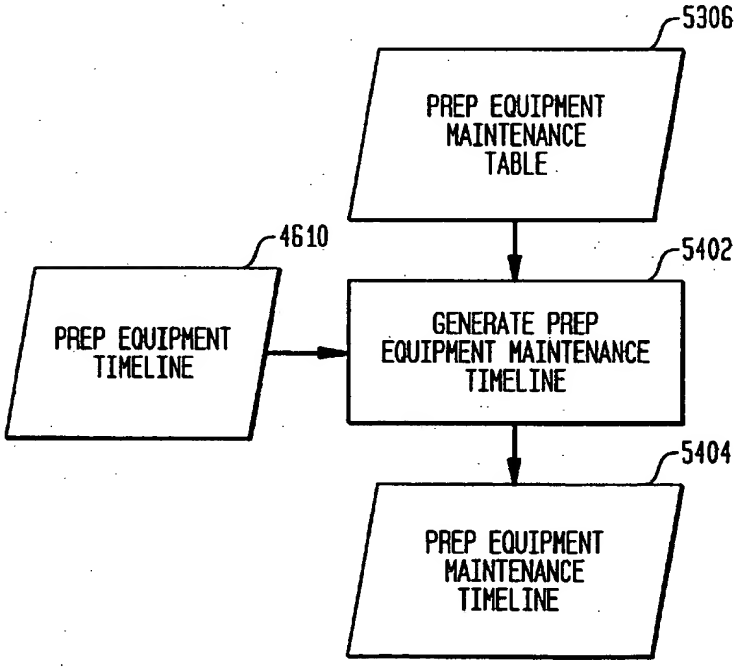


FIG. 54



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Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 55

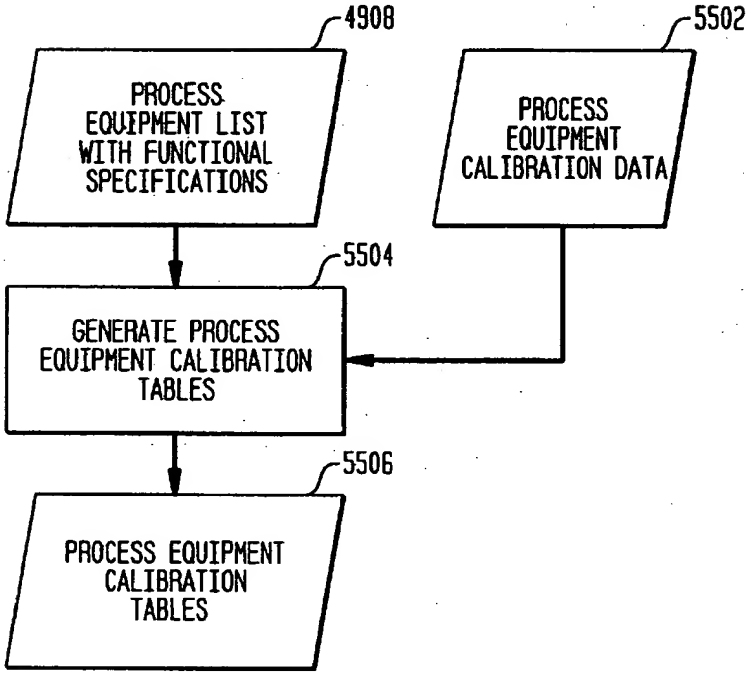
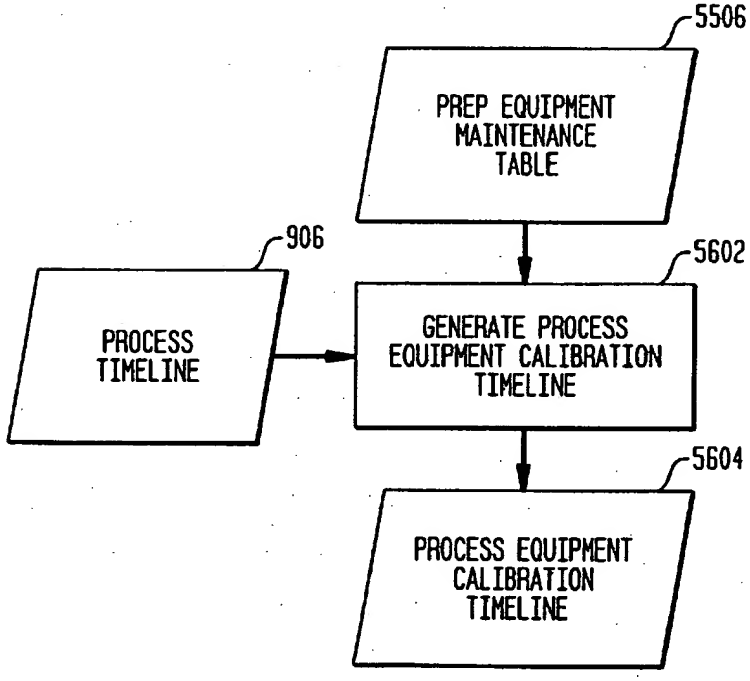


FIG. 56



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For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 57

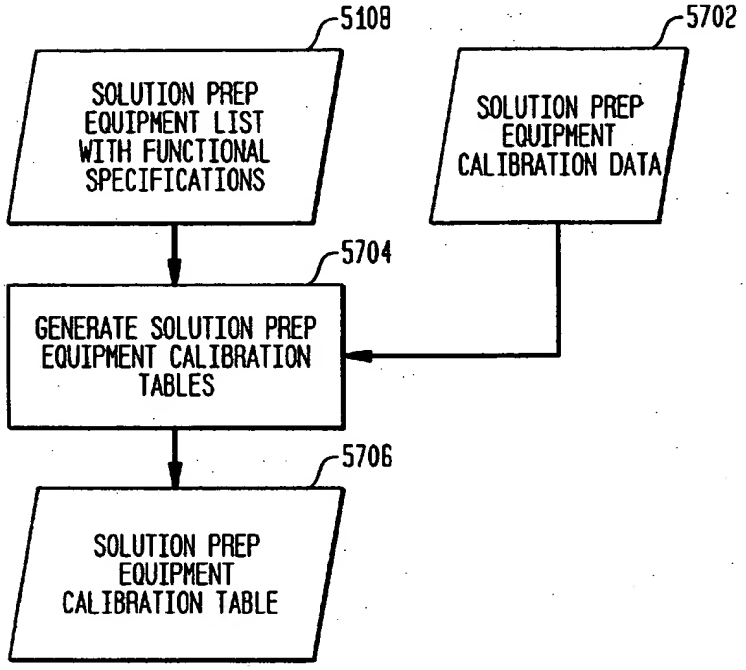
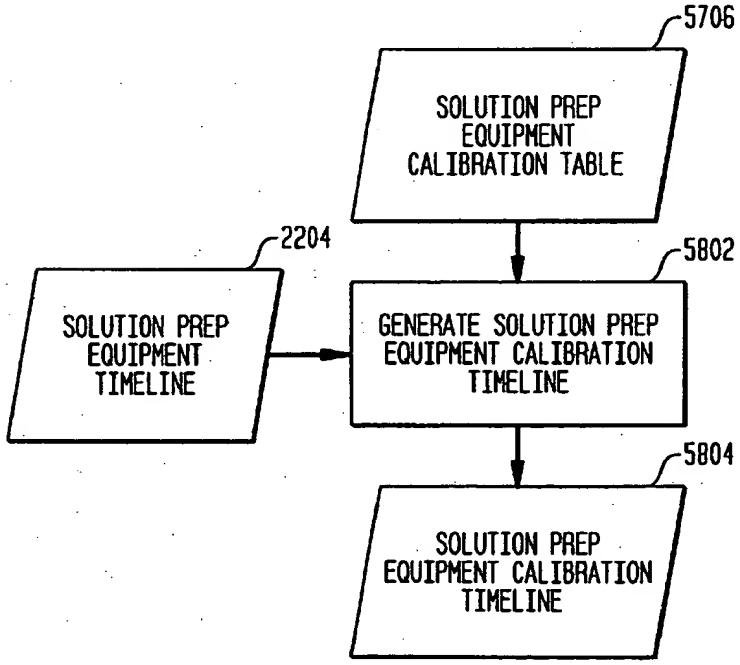


FIG. 58



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For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 59

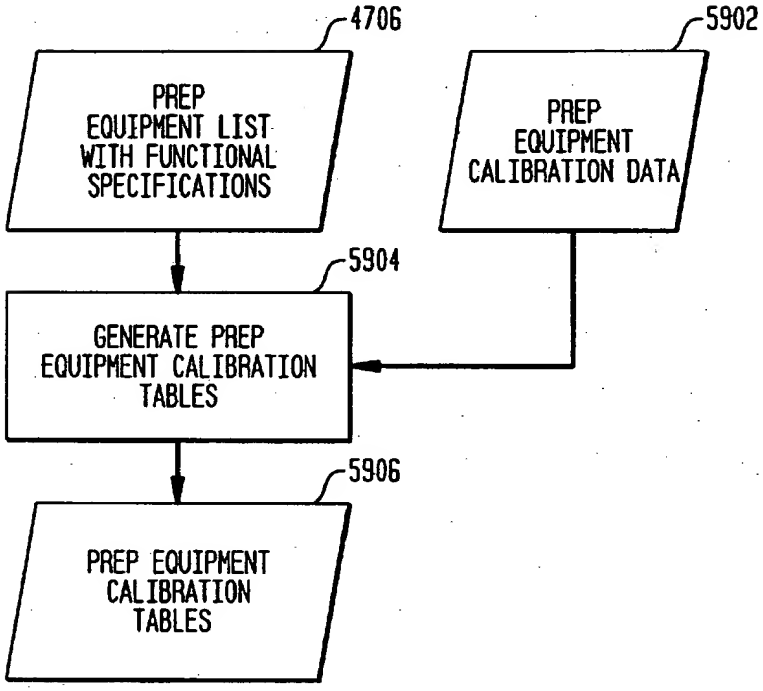
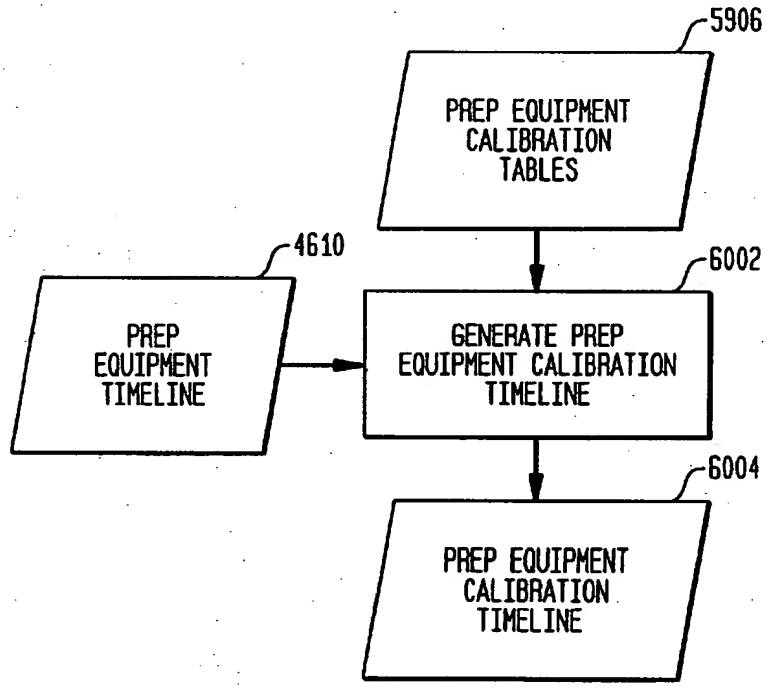


FIG. 60



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(As Amended)

FIG. 61

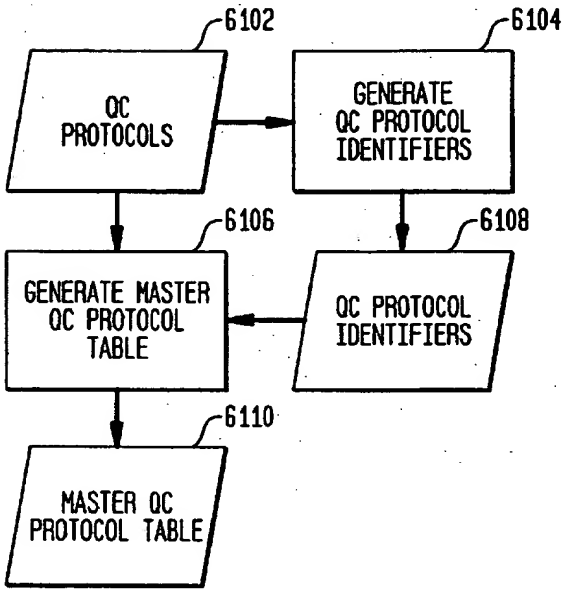
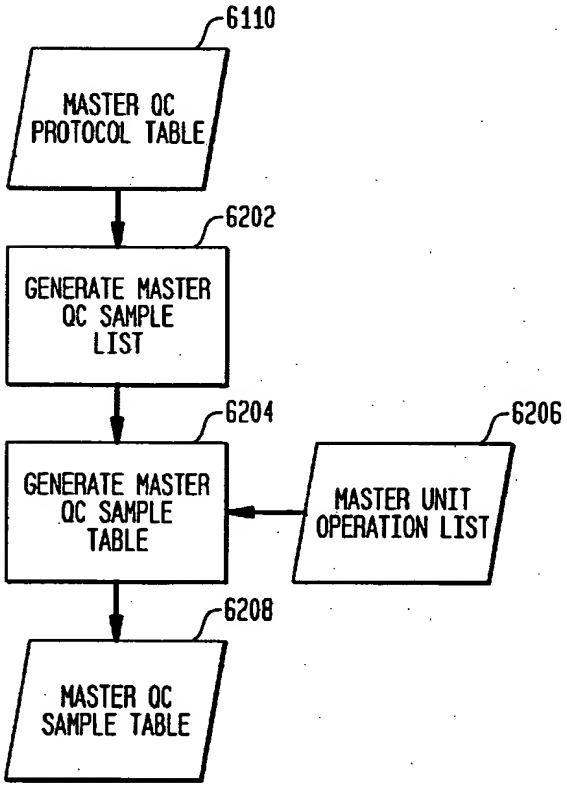


FIG. 62



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For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 63

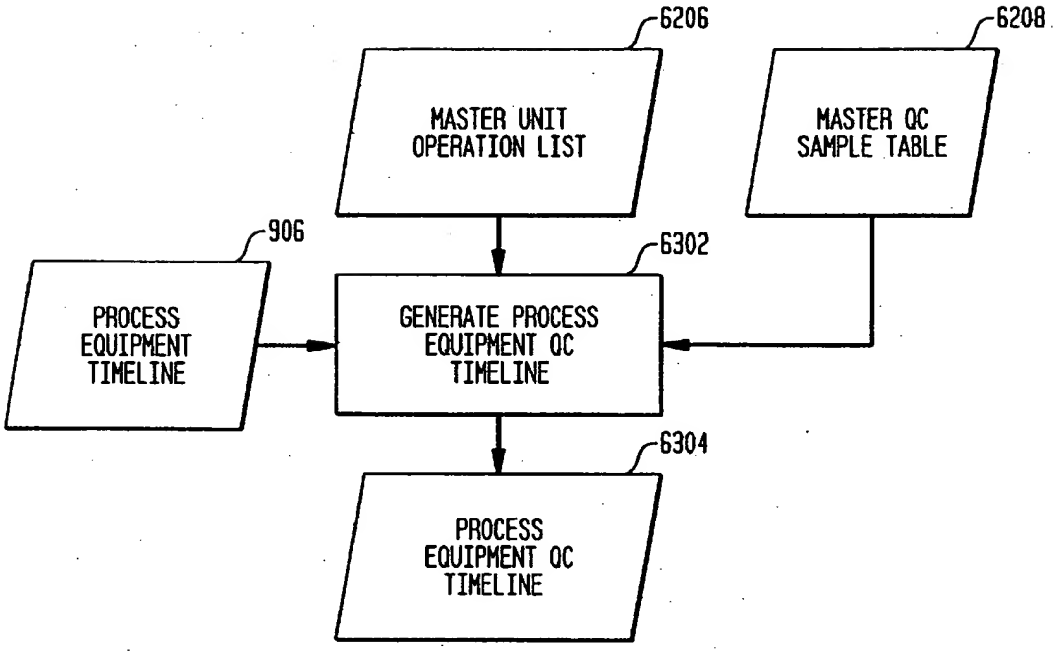

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FIG. 64A-1

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

6402 6404

Equipment Items	Filters					
	Materials					Labor
	Item No.	Qty	Cycle Life	Unit Cost	$/Cycle	Hours
1 Inoculum Prep						
-80 C Stock Freezer						
Shaking Water Bath						
2 Flask Growth						
Floor Incubator-Shaker						
Microscope						
3 Seed Fermentation						
Seed Bioreactor						
4 Fermentation						
Production Bioreactor	75868	1	100	55	.55	.5
5 Whole Cell Harvest						
Harvest Heat Exchanger						
Harvest Vessel						
Agitator						
6 Cell Concentration						
Pump						
Filter Holder						
Manifolding						
Instrumentation						
MF Flush Vessel						
MF Prime Vessel						
MF Filtrate Vessel						
Agitator						
MF Wash Vessel						
MF Regeneration Vessel						
MF Storage Vessel						

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FIG. 64A-2

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

	6406							6408
	Gaskets							Bearings
	Materials					Labor		Materials
$/Cycle	Item No.	Qty	Cycle Life	Unit Cost	$/Cycle	Hours	$/Cycle	Item No.
.0875	48994	1	500	55	.11	1	.035	
	62589	1	350	85	.2429	1	.05	

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FIG. 64B-1

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

6408

Equipment Items	Qty	Cycle Life	Unit Cost	$/Cycle	Labor Hours
1 Inoculum Prep					
-80 C Stock Freezer					
Shaking Water Bath					
2 Flask Growth					
Floor Incubator-Shaker					
Microscope					
3 Seed Fermentation					
Seed Bioreactor					
4 Fermentation					
Production Bioreactor					
5 Whole Cell Harvest					
Harvest Heat Exchanger					
Harvest Vessel					
Agitator					
6 Cell Concentration					
Pump					
Filter Holder					
Manifolding					
Instrumentation					
MF Flush Vessel					
MF Prime Vessel					
MF Filtrate Vessel					
Agitator					
MF Wash Vessel					
MF Regeneration Vessel					
MF Storage Vessel					

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(As Amended)

FIG. 64B-2

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

6410 6412

	Seals							Belts	
	Materials					Labor		Materials	
$/Cycle	Item No.	Qty	Cycle Life	Unit Cost	$/Cycle	Hours	$/Cycle	Item No.	Qty
	54812	2	250	12	.048	1	.07		
	48695	1	250	18.9	.0756	1	.07		
								85258	1

FIG. 64C-1

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

6414

Equipment Items	Cycle Life	Unit Cost	$/Cycle	Labor Hours
1 Inoculum Prep				
-80 C Stock Freezer				
Shaking Water Bath				
2 Flask Growth				
Floor Incubator-Shaker				
Microscope				
3 Seed Fermentation				
Seed Bioreactor				
4 Fermentation				
Production Bioreactor	500	25	.05	1
5 Whole Cell Harvest				
Harvest Heat Exchanger				
Harvest Vessel				
Agitator				
6 Cell Concentration				
Pump				
Filter Holder				
Manifolding				
Instrumentation				
MF Flush Vessel				
MF Prime Vessel				
MF Filtrate Vessel				
Agitator				
MF Wash Vessel				
MF Regeneration Vessel				
MF Storage Vessel				

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(As Amended)

FIG. 64C-2

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

	6416							6418		
	Shafts							Lubricant		
	Materials					Labor		Materials		
$/Cycle	Item No.	Qty	Cycle Life	Unit Cost	$/Cycle	Hours	$/Cycle	Item No.	Qty	Cycle Life
								78954	.5	
.035										

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(As Amended)

FIG. 64D-1

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

6418

Equipment Items	Unit Cost	$/Cycle	Labor Hours
1 Inoculum Prep			
-80 C Stock Freezer			
Shaking Water Bath			
2 Flask Growth			
Floor Incubator-Shaker			
Microscope			
3 Seed Fermentation			
Seed Bioreactor	1.5	.03	.5
4 Fermentation			
Production Bioreactor			
5 Whole Cell Harvest			
Harvest Heat Exchanger			
Harvest Vessel			
Agitator			
6 Cell Concentration			
Pump			
Filter Holder			
Manifolding			
Instrumentation			
MF Flush Vessel			
MF Prime Vessel			
MF Filtrate Vessel			
Agitator			
MF Wash Vessel			
MF Regeneration Vessel			
MF Storage Vessel			

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(As Amended)

FIG. 64D-2

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

6420

	Thermal Media						
	Materials					Labor	
$/Cycle	Item No.	Qty	Cycle Life	Unit Cost	$/Cycle	Hours	$/Cycle
.175							
	56258	5	500	.85	425	1	17.5

FIG. 64E-1

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

Equipment Items	Filters					
	Materials					Labor
	Item No.	Qty	Cycle Life	Unit Cost	$/Cycle	Hours
7 Cell Concentration 2						
MF Wash Vessel						
Pump						
Filter Holder						
Manifolding						
Instrumentation						
MF Flush Vessel						
MF Prime Vessel						
MF Filtrate Vessel						
MF Wash Vessel						
MF Regeneration Vessel						
MF Storage Vessel						
8 Cell Resuspension						
Resuspension Vessel						
Stir Plate						
9 Cell Disruption						
Cell Disruptor						
Lysate Vessel						
10 IB Resuspension 1&2						
Resuspension Vessel						
Stir Plate						
11 IB Concentration 1&2						
MF Wash Vessel						
Pump						
Filter Holder						

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For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 64E-2

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

	Gaskets							Bearings
	Materials					Labor		Materials
$/Cycle	Item No.	Qty	Cycle Life	Unit Cost	$/Cycle	Hours	$/Cycle	Item No.

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For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 64F-1

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

Equipment Items	Qty	Cycle Life	Unit Cost	$/Cycle	Labor Hours
7 Cell Concentration 2					
MF Wash Vessel					
Pump					
Filter Holder					
Manifolding					
Instrumentation					
MF Flush Vessel					
MF Prime Vessel					
MF Filtrate Vessel					
MF Wash Vessel					
MF Regeneration Vessel					
MF Storage Vessel					
8 Cell Resuspension					
Resuspension Vessel					
Stir Plate					
9 Cell Disruption					
Cell Disruptor					
Lysate Vessel					
10 IB Resuspension 1&2					
Resuspension Vessel					
Stir Plate					
11 IB Concentration 1&2					
MF Wash Vessel					
Pump					
Filter Holder					

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For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 64F-2

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

	Seals							Belts	
	Materials					Labor		Materials	
$/Cycle	Item No.	Qty	Cycle Life	Unit Cost	$/Cycle	Hours	$/Cycle	Item No.	Qty

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Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
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(As Amended)

FIG. 64G-1

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

Equipment Items	Cycle Life	Unit Cost	$/Cycle	Labor Hours
7 Cell Concentration 2				
MF Wash Vessel				
Pump				
Filter Holder				
Manifolding				
Instrumentation				
MF Flush Vessel				
MF Prime Vessel				
MF Filtrate Vessel				
MF Wash Vessel				
MF Regeneration Vessel				
MF Storage Vessel				
8 Cell Resuspension				
Resuspension Vessel				
Stir Plate				
9 Cell Disruption				
Cell Disruptor				
Lysate Vessel				
10 IB Resuspension 1&2				
Resuspension Vessel				
Stir Plate				
11 IB Concentration 1&2				
MF Wash Vessel				
Pump				
Filter Holder				

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Dkt No. : 1606.0020004; Group Unit: 2128
Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 64G-2

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

	Shafts							Lubricant		
	Materials					Labor		Materials		
$/Cycle	Item No.	Qty	Cycle Life	Unit Cost	$/Cycle	Hours	$/Cycle	Item No.	Qty	Cycle Life

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(As Amended)

FIG. 64H-1

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

Equipment Items	Unit Cost	$/Cycle	Labor Hours
7 Cell Concentration 2			
MF Wash Vessel			
Pump			
Filter Holder			
Manifolding			
Instrumentation			
MF Flush Vessel			
MF Prime Vessel			
MF Filtrate Vessel			
MF Wash Vessel			
MF Regeneration Vessel			
MF Storage Vessel			
8 Cell Resuspension			
Resuspension Vessel			
Stir Plate			
9 Cell Disruption			
Cell Disruptor			
Lysate Vessel			
10 IB Resuspension 1&2			
Resuspension Vessel			
Stir Plate			
11 IB Concentration 1&2			
MF Wash Vessel			
Pump			
Filter Holder			

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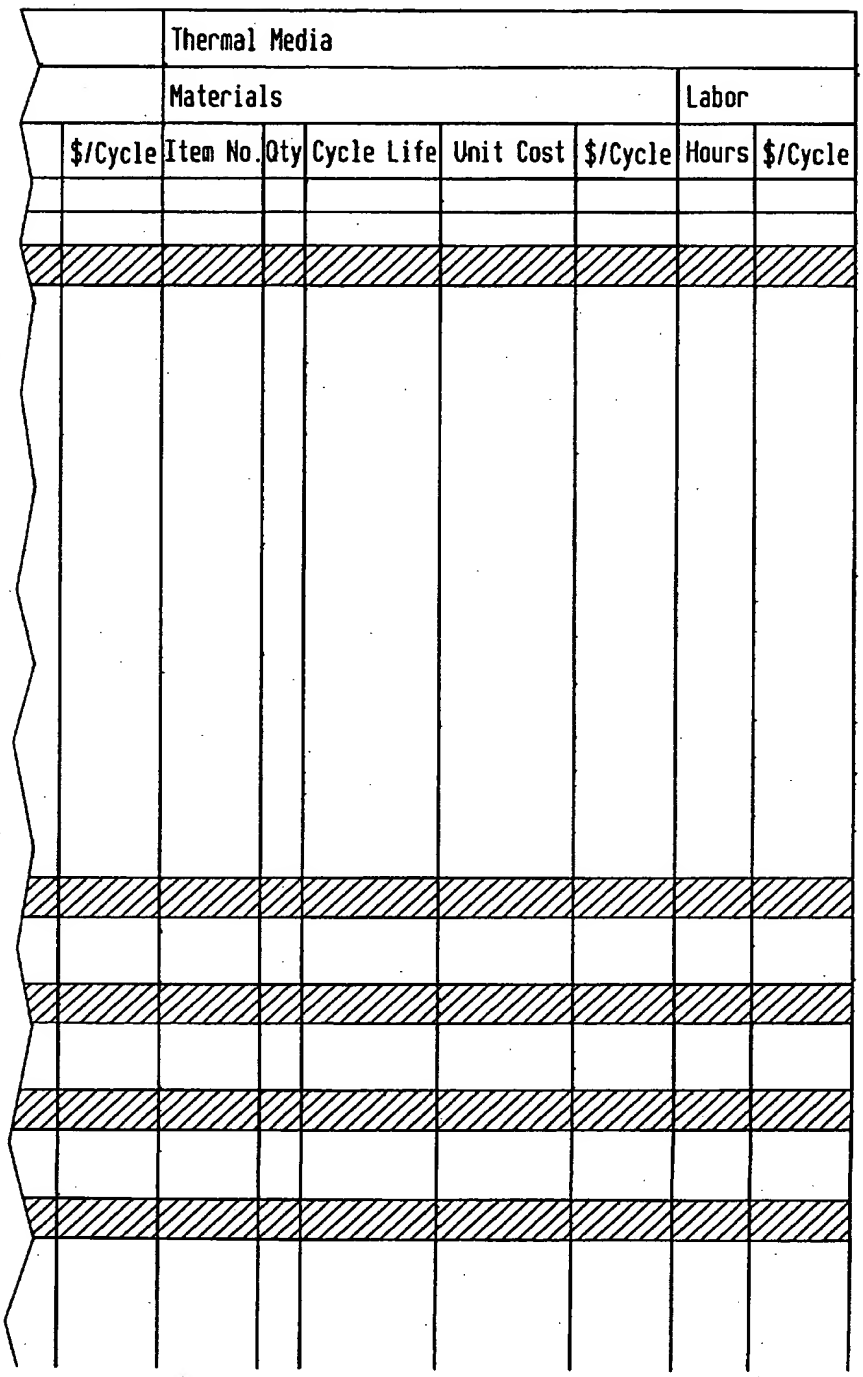
For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 64H-2

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION



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For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 64I-1

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

Equipment Items	Filters					
	Materials					Labor
	Item No.	Qty	Cycle Life	Unit Cost	$/Cycle	Hours
Manifolding						
Instrumentation						
MF Flush Vessel						
MF Prime Vessel						
MF Filtrate Vessel						
MF Dilute Vessel						
MF Wash Vessel						
MF Regeneration Vessel						
MF Storage Vessel						
14 Renaturation						
Renaturant Vessel						
Stir Plate						
15 Buffer Exchange						
Pump						
Filter Holder						
Manifolding						
Instrumentation						
UF Flush Vessel						
UF Prime Vessel						
UF Filtrate Vessel						
UF Wash Vessel						
UF Diluent Vessel						
UF Regeneration Vessel						
UF Storage Vessel						

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(As Amended)

FIG. 64I-2

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

	Gaskets							Bearings	
	Materials					Labor		Materials	
	$/Cycle	Item No.	Qty	Cycle Life	Unit Cost	$/Cycle	Hours	$/Cycle	Item No.

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(As Amended)

FIG. 64J-1

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

Equipment Items	Qty	Cycle Life	Unit Cost	$/Cycle	Labor Hours
Manifolding					
Instrumentation					
MF Flush Vessel					
MF Prime Vessel					
MF Filtrate Vessel					
MF Dilute Vessel					
MF Wash Vessel					
MF Regeneration Vessel					
MF Storage Vessel					
14 Renaturation					
Renaturant Vessel					
Stir Plate					
15 Buffer Exchange					
Pump					
Filter Holder					
Manifolding					
Instrumentation					
UF Flush Vessel					
UF Prime Vessel					
UF Filtrate Vessel					
UF Wash Vessel					
UF Diluent Vessel					
UF Regeneration Vessel					
UF Storage Vessel					

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(As Amended)

FIG. 64J-2

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

	Seals							Belts	
	Materials					Labor		Materials	
$/Cycle	Item No.	Qty	Cycle Life	Unit Cost	$/Cycle	Hours	$/Cycle	Item No.	Qty

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(As Amended)

FIG. 64K-1

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

Equipment Items	Cycle Life	Unit Cost	$/Cycle	Labor Hours
Manifolding				
Instrumentation				
MF Flush Vessel				
MF Prime Vessel				
MF Filtrate Vessel				
MF Dilute Vessel				
MF Wash Vessel				
MF Regeneration Vessel				
MF Storage Vessel				
14 Renaturation				
Renaturant Vessel				
Stir Plate				
15 Buffer Exchange				
Pump				
Filter Holder				
Manifolding				
Instrumentation				
UF Flush Vessel				
UF Prime Vessel				
UF Filtrate Vessel				
UF Wash Vessel				
UF Diluent Vessel				
UF Regeneration Vessel				
UF Storage Vessel				

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For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 64K-2

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

	Shafts							Lubricant		
	Materials					Labor		Materials		
$/Cycle	Item No.	Qty	Cycle Life	Unit Cost	$/Cycle	Hours	$/Cycle	Item No.	Qty	Cycle Life

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For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 64L-1

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

Equipment Items	Unit Cost	$/Cycle	Labor Hours
Manifolding			
Instrumentation			
MF Flush Vessel			
MF Prime Vessel			
MF Filtrate Vessel			
MF Dilute Vessel			
MF Wash Vessel			
MF Regeneration Vessel			
MF Storage Vessel			
14 Renaturation			
Renaturant Vessel			
Stir Plate			
15 Buffer Exchange			
Pump			
Filter Holder			
Manifolding			
Instrumentation			
UF Flush Vessel			
UF Prime Vessel			
UF Filtrate Vessel			
UF Wash Vessel			
UF Diluent Vessel			
UF Regeneration Vessel			
UF Storage Vessel			

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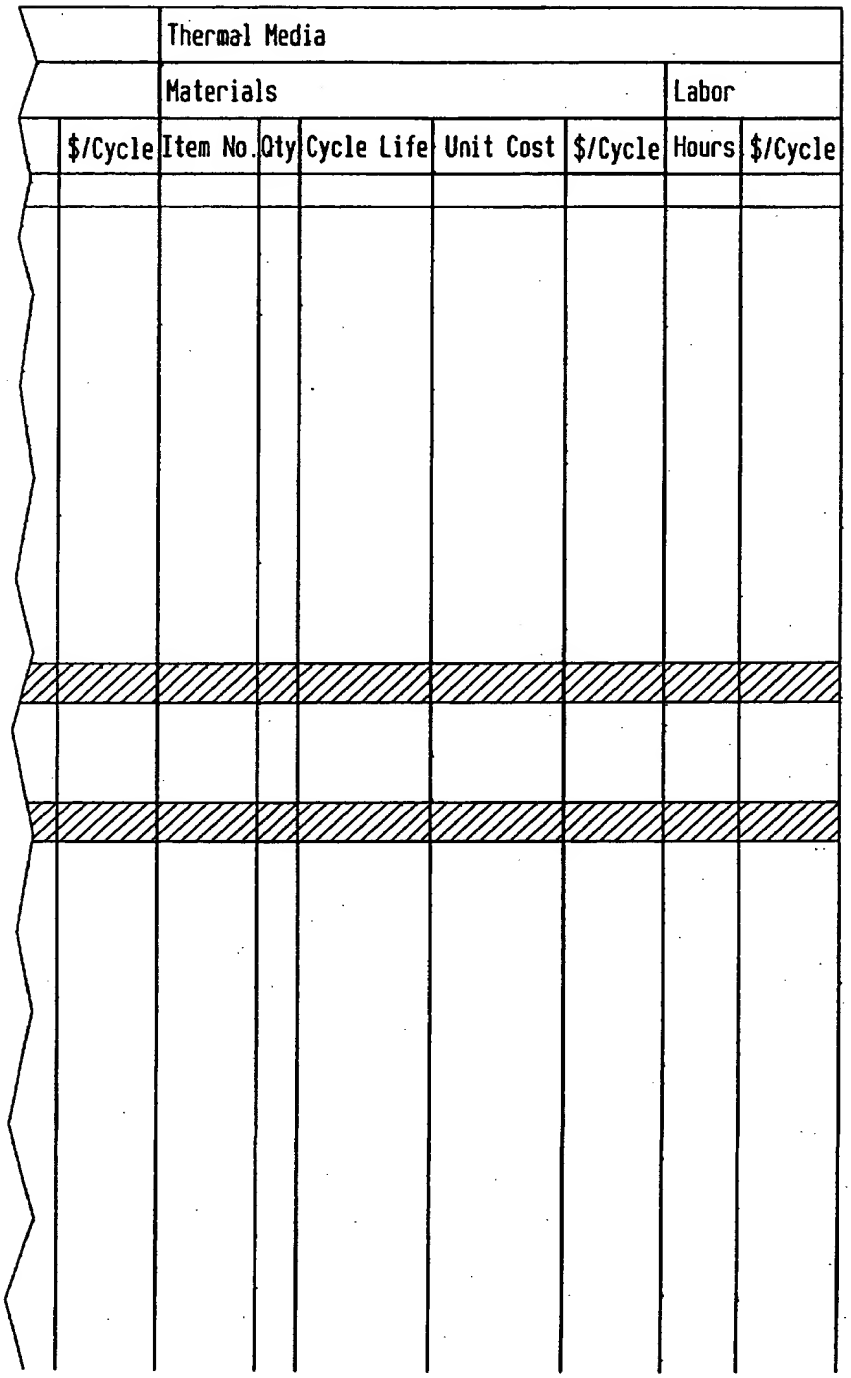
(As Amended)

FIG. 64L-2

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION



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(As Amended)

FIG. 64M-1

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

	Filters					
	Materials					Labor
Equipment Items	Item No.	Qty	Cycle Life	Unit Cost	$/Cycle	Hours
UF Waste Vessel						
16 Chromatography 1						
Chromatography Column						
Pump						
Inst.& Control System						
Manifolding						
Equilibration Vessel						
Wash Vessel						
Eluent Vessel						
Regenerate Vessel						
Storage Vessel						
Waste Vessel(1)						
Product Vessel						
Waste Vessel(2)						
17 Chromatography 2						
Chromatography Column						
Pump						
Inst.& Control System						
Manifolding						
Equilibration Vessel						
Wash Vessel						
Eluent Vessel						
Regenerate Vessel						

Appl. No. : 09/100,088; Filed: June 19, 1998
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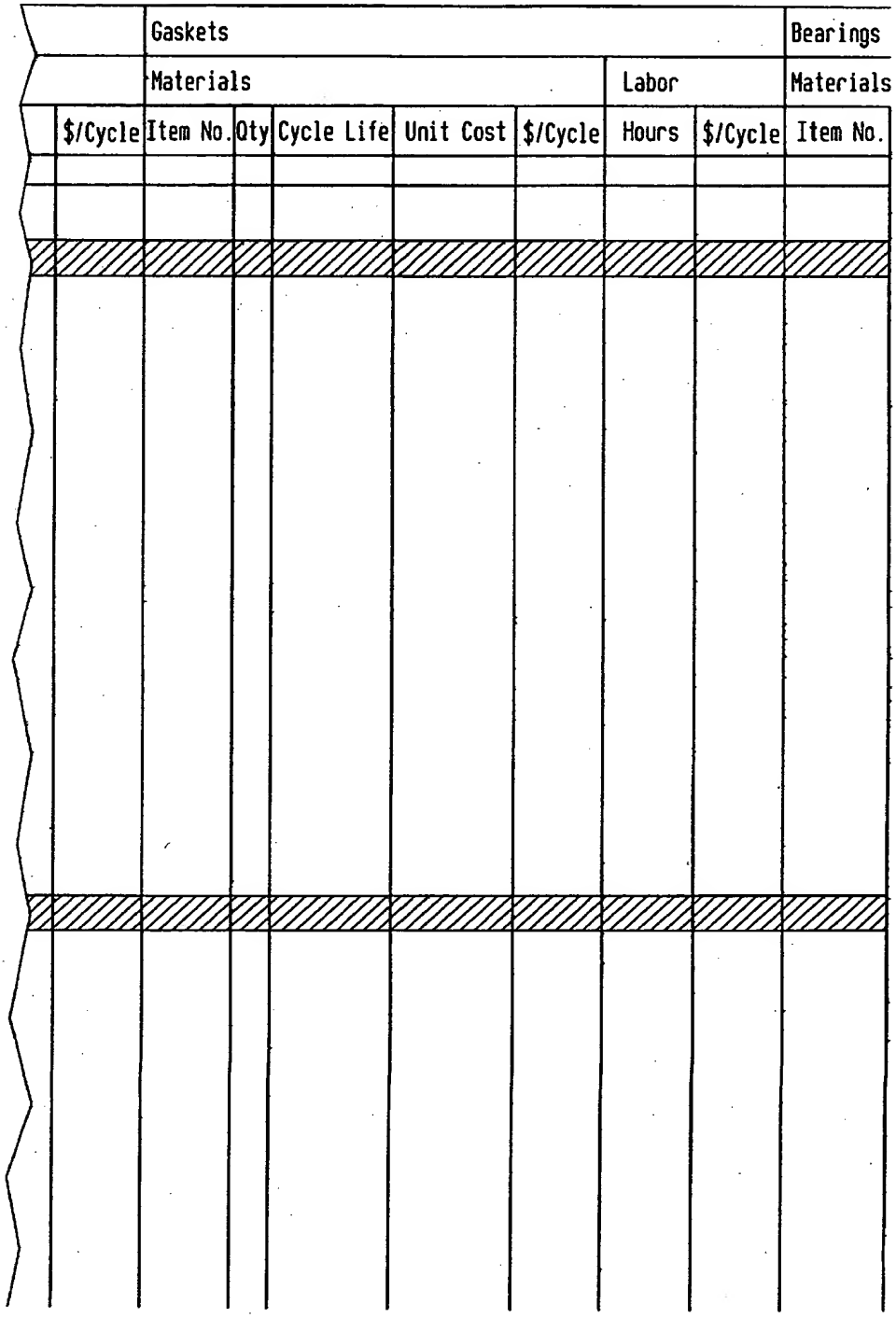
For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 64M-2

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION



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(As Amended)

FIG. 64N-1

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

Equipment Items	Qty	Cycle Life	Unit Cost	$/Cycle	Labor Hours
UF Waste Vessel					
16 Chromatography 1					
Chromatography Column					
Pump					
Inst.& Control System					
Manifolding					
Equilibration Vessel					
Wash Vessel					
Eluent Vessel					
Regenerate Vessel					
Storage Vessel					
Waste Vessel(1)					
Product Vessel					
Waste Vessel(2)					
17 Chromatography 2					
Chromatography Column					
Pump					
Inst.& Control System					
Manifolding					
Equilibration Vessel					
Wash Vessel					
Eluent Vessel					
Regenerate Vessel					

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(As Amended)

FIG. 64N-2

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

		Seals							Belts	
		Materials					Labor		Materials	
	$/Cycle	Item No.	Qty	Cycle Life	Unit Cost	$/Cycle	Hours	$/Cycle	Item No.	Qty

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(As Amended)

FIG. 640-1

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

Equipment Items	Cycle Life	Unit Cost	$/Cycle	Labor Hours
UF Waste Vessel				
16 Chromatography 1				
Chromatography Column				
Pump				
Inst.& Control System				
Manifolding				
Equilibration Vessel				
Wash Vessel				
Eluent Vessel				
Regenerate Vessel				
Storage Vessel				
Waste Vessel(1)				
Product Vessel				
Waste Vessel(2)				
17 Chromatography 2				
Chromatography Column				
Pump				
Inst.& Control System				
Manifolding				
Equilibration Vessel				
Wash Vessel				
Eluent Vessel				
Regenerate Vessel				

Appl. No. : 09/100,088; Filed: June 19, 1998
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For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 640-2

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

	Shafts							Lubricant		
	Materials					Labor		Materials		
$/Cycle	Item No.	Qty	Cycle Life	Unit Cost	$/Cycle	Hours	$/Cycle	Item No.	Qty	Cycle Life

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(As Amended)

FIG. 64P-1

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

Equipment Items	Unit Cost	$/Cycle	Labor Hours
UF Waste Vessel			
16 Chromatography 1			
Chromatography Column			
Pump			
Inst.& Control System			
Manifolding			
Equilibration Vessel			
Wash Vessel			
Eluent Vessel			
Regenerate Vessel			
Storage Vessel			
Waste Vessel(1)			
Product Vessel			
Waste Vessel(2)			
17 Chromatography 2			
Chromatography Column			
Pump			
Inst.& Control System			
Manifolding			
Equilibration Vessel			
Wash Vessel			
Eluent Vessel			
Regenerate Vessel			

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(As Amended)

FIG. 64P-2

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

	Thermal Media						
	Materials					Labor	
$/Cycle	Item No.	Qty	Cycle Life	Unit Cost	$/Cycle	Hours	$/Cycle

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For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 640-1

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

Equipment Items	Filters					
	Materials					Labor
	Item No.	Qty	Cycle Life	Unit Cost	$/Cycle	Hours
Storage Vessel						
Waste Vessel(1)						
Product Vessel						
Waste Vessel(2)						
18 Buffer Exchange						
Pump						
Filter Holder						
Manifolding						
Instrumentation						
UF Flush Vessel						
UF Prime Vessel						
UF Filtrate Vessel						
UF Wash Vessel						
UF Diluent Vessel						
UF Regeneration Vessel						
UF Storage Vessel						
UF Waste Vessel						
19 Chromatography 3						
Chromatography Column						
Pump						
Inst.& Control System						
Manifolding						
Equilibration Vessel						

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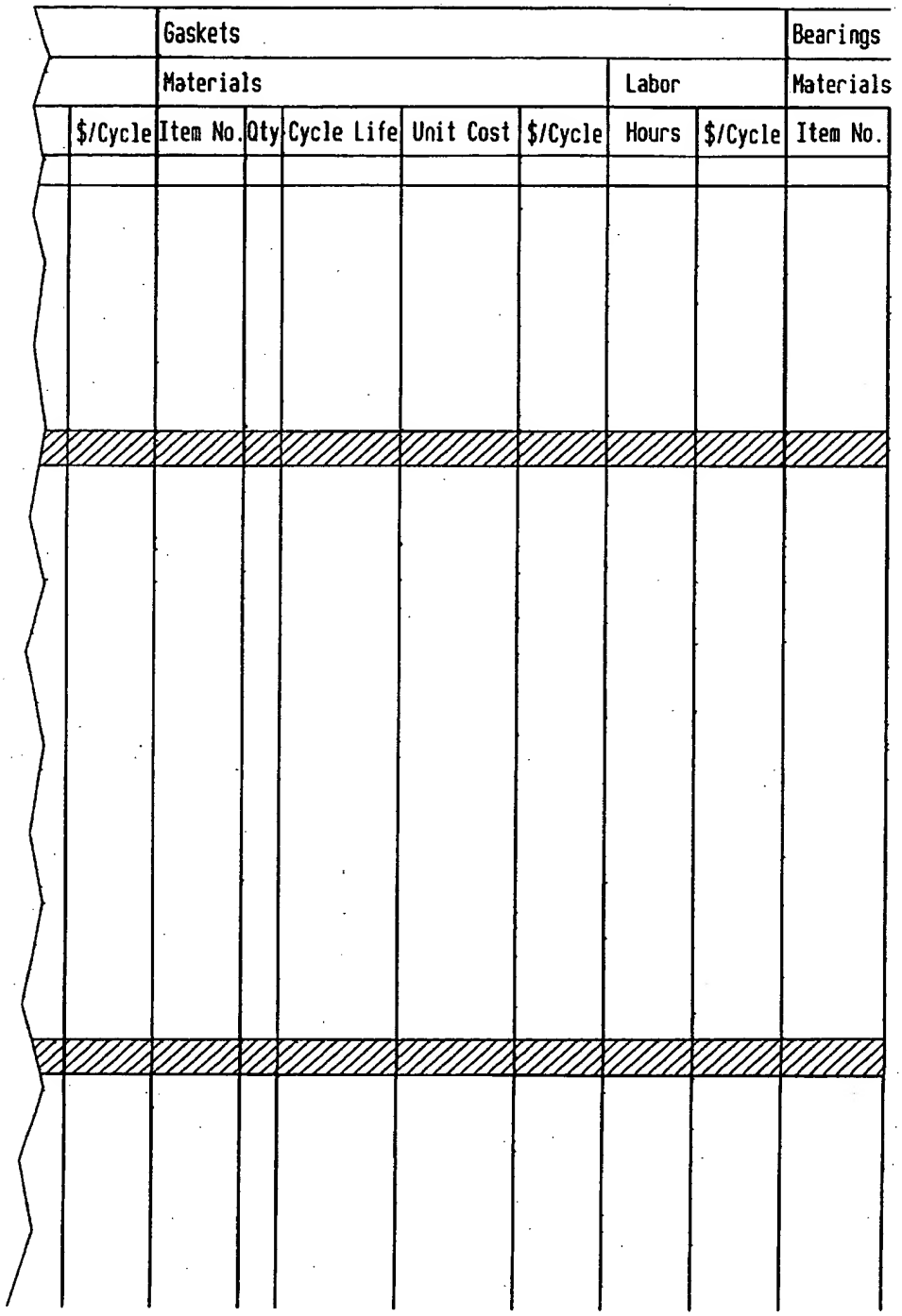
For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 64Q-2

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION



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(As Amended)

FIG. 64R-1

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

Equipment Items	Qty	Cycle Life	Unit Cost	$/Cycle	Labor Hours
Storage Vessel					
Waste Vessel(1)					
Product Vessel					
Waste Vessel(2)					
18 Buffer Exchange					
Pump					
Filter Holder					
Manifolding					
Instrumentation					
UF Flush Vessel					
UF Prime Vessel					
UF Filtrate Vessel					
UF Wash Vessel					
UF Diluent Vessel					
UF Regeneration Vessel					
UF Storage Vessel					
UF Waste Vessel					
19 Chromatography 3					
Chromatography Column					
Pump					
Inst.& Control System					
Manifolding					
Equilibration Vessel					

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(As Amended)

FIG. 64R-2

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

		Seals							Belts	
		Materials					Labor		Materials	
	$/Cycle	Item No.	Qty	Cycle Life	Unit Cost	$/Cycle	Hours	$/Cycle	Item No.	Qty

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For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 64S-1

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

Equipment Items	Cycle Life	Unit Cost	$/Cycle	Labor Hours
Storage Vessel				
Waste Vessel(1)				
Product Vessel				
Waste Vessel(2)				
18 Buffer Exchange				
Pump				
Filter Holder				
Manifolding				
Instrumentation				
UF Flush Vessel				
UF Prime Vessel				
UF Filtrate Vessel				
UF Wash Vessel				
UF Diluent Vessel				
UF Regeneration Vessel				
UF Storage Vessel				
UF Waste Vessel				
19 Chromatography 3				
Chromatography Column				
Pump				
Inst.& Control System				
Manifolding				
Equilibration Vessel				

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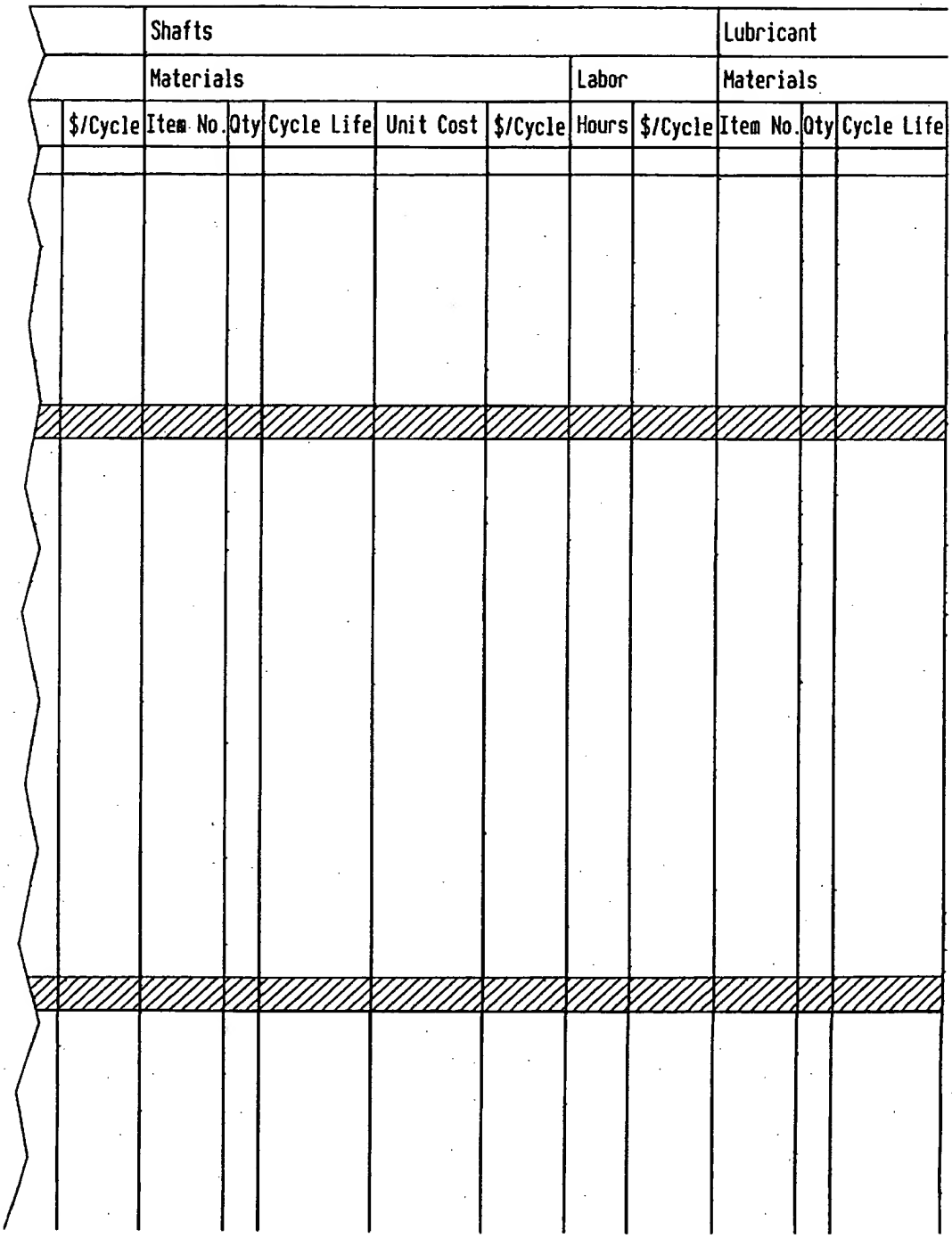
(As Amended)

FIG. 64S-2

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION



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Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 64T-1

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

Equipment Items	Unit Cost	$/Cycle	Labor Hours
Storage Vessel			
Waste Vessel(1)			
Product Vessel			
Waste Vessel(2)			
18 Buffer Exchange			
Pump			
Filter Holder			
Manifolding			
Instrumentation			
UF Flush Vessel			
UF Prime Vessel			
UF Filtrate Vessel			
UF Wash Vessel			
UF Diluent Vessel			
UF Regeneration Vessel			
UF Storage Vessel			
UF Waste Vessel			
19 Chromatography 3			
Chromatography Column			
Pump			
Inst.& Control System			
Manifolding			
Equilibration Vessel			

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(As Amended)

FIG. 64T-2

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

	Thermal Media						
	Materials					Labor	
$/Cycle	Item No.	Qty	Cycle Life	Unit Cost	$/Cycle	Hours	$/Cycle

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(As Amended)

FIG. 64U-1

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

Equipment Items	Filters					
	Materials					Labor
	Item No.	Qty	Cycle Life	Unit Cost	$/Cycle	Hours
Wash Vessel						
Eluent Vessel						
Regenerate Vessel						
Storage Vessel						
Waste Vessel(1)						
Product Vessel						
Waste Vessel(2)						
20 Buffer Exchange						
Pump						
Filter Holder						
Manifolding						
Instrumentation						
UF Flush Vessel						
UF Prime Vessel						
UF Filtrate Vessel						
UF Wash Vessel						
UF Diluent Vessel						
UF Regeneration Vessel						
UF Storage Vessel						
UF Waste Vessel						
21 Chromatography 4						
Chromatography Column						
Pump						

Appl. No. : 09/100,088; Filed: June 19, 1998
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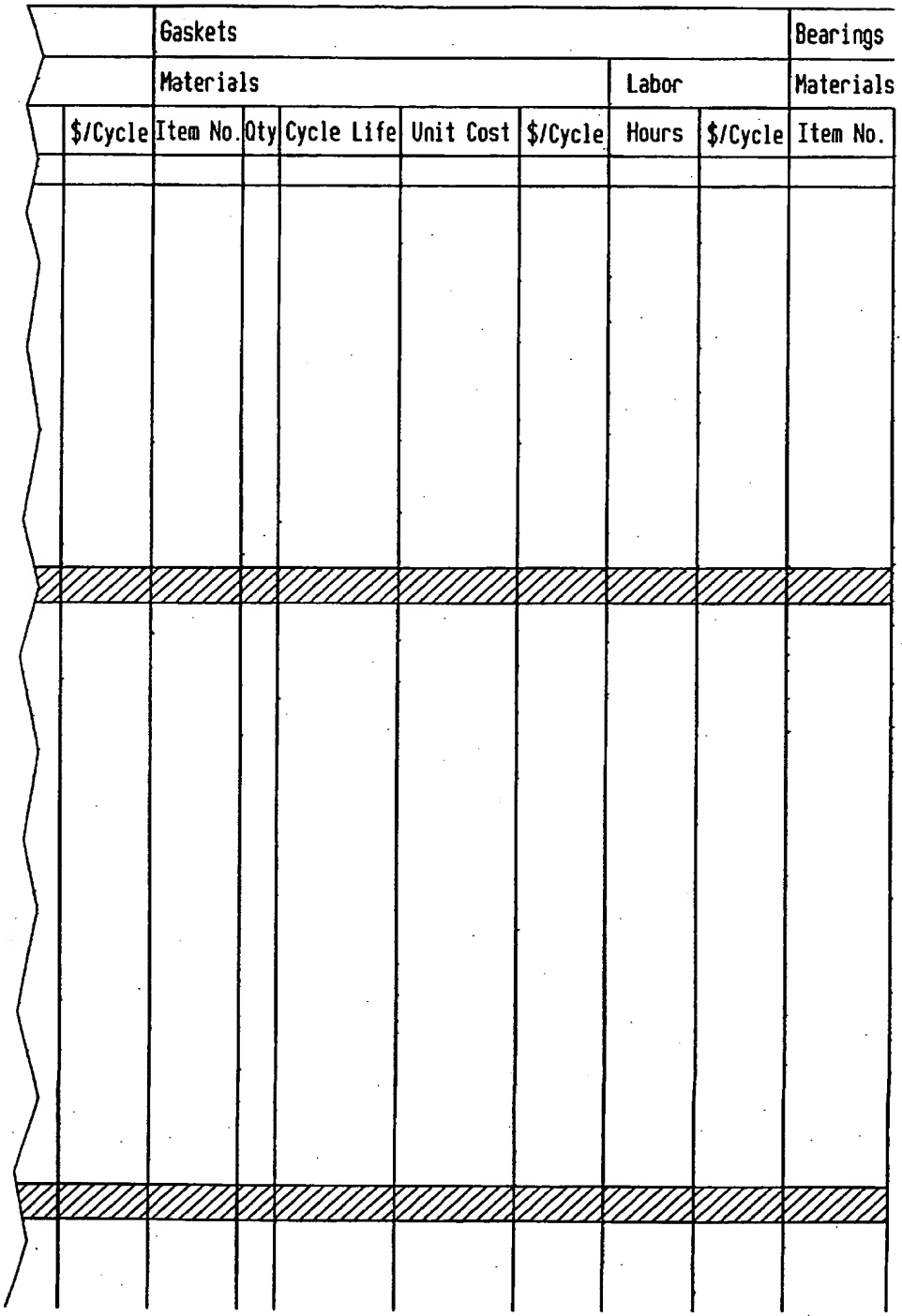
For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 64U-2

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION



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Inventor: Peter G. BROWN; Tel. No.: 202-371-2600

FIG. 64V-1

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

Equipment Items	Qty	Cycle Life	Unit Cost	$/Cycle	Labor Hours
Wash Vessel					
Eluent Vessel					
Regenerate Vessel					
Storage Vessel					
Waste Vessel(1)					
Product Vessel					
Waste Vessel(2)					
20 Buffer Exchange					
Pump					
Filter Holder					
Manifolding					
Instrumentation					
UF Flush Vessel					
UF Prime Vessel					
UF Filtrate Vessel					
UF Wash Vessel					
UF Diluent Vessel					
UF Regeneration Vessel					
UF Storage Vessel					
UF Waste Vessel					
21 Chromatography 4					
Chromatography Column					
Pump					

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(As Amended)

FIG. 64V-2

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

	Seals							Belts	
	Materials					Labor		Materials	
$/Cycle	Item No.	Qty	Cycle Life	Unit Cost	$/Cycle	Hours	$/Cycle	Item No.	Qty

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(As Amended)

FIG. 64W-1

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

Equipment Items	Cycle Life	Unit Cost	$/Cycle	Labor Hours
Wash Vessel				
Eluent Vessel				
Regenerate Vessel				
Storage Vessel				
Waste Vessel(1)				
Product Vessel				
Waste Vessel(2)				
20 Buffer Exchange				
Pump				
Filter Holder				
Manifolding				
Instrumentation				
UF Flush Vessel				
UF Prime Vessel				
UF Filtrate Vessel				
UF Wash Vessel				
UF Diluent Vessel				
UF Regeneration Vessel				
UF Storage Vessel				
UF Waste Vessel				
21 Chromatography 4				
Chromatography Column				
Pump				

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(As Amended)

FIG. 64W-2

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

	Shafts							Lubricant		
	Materials					Labor		Materials		
$/Cycle	Item No.	Qty	Cycle Life	Unit Cost	$/Cycle	Hours	$/Cycle	Item No.	Qty	Cycle Life

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(As Amended)

FIG. 64X-1

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

Equipment Items	Unit Cost	$/Cycle	Labor Hours
Wash Vessel			
Eluent Vessel			
Regenerate Vessel			
Storage Vessel			
Waste Vessel(1)			
Product Vessel			
Waste Vessel(2)			
20 Buffer Exchange			
Pump			
Filter Holder			
Manifolding			
Instrumentation			
UF Flush Vessel			
UF Prime Vessel			
UF Filtrate Vessel			
UF Wash Vessel			
UF Diluent Vessel			
UF Regeneration Vessel			
UF Storage Vessel			
UF Waste Vessel			
21 Chromatography 4			
Chromatography Column			
Pump			

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FIG. 64X-2

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

	Thermal Media						
	Materials					Labor	
$/Cycle	Item No.	Qty	Cycle Life	Unit Cost	$/Cycle	Hours	$/Cycle

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FIG. 64Y-1

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

	Filters					
	Materials					Labor
Equipment Items	Item No.	Qty	Cycle Life	Unit Cost	$/Cycle	Hours
Inst.& Control System						
Manifolding						
Equilibration Vessel						
Wash Vessel						
Eluent Vessel						
Regenerate Vessel						
Storage Vessel						
Waste Vessel(1)						
Product Vessel						
Waste Vessel(2)						
22 Sterile Filtration						
MF Wash Vessel						
Pump						
Filter Holder						
Manifolding						
Instrumentation						
MF Flush Vessel						
MF Prime Vessel						
MF Filtrate Vessel						
MF Wash Vessel						

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FIG. 64Y-2

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

	Gaskets							Bearings
	Materials					Labor		Materials
$/Cycle	Item No.	Qty	Cycle Life	Unit Cost	$/Cycle	Hours	$/Cycle	Item No.

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(As Amended)

FIG. 64Z-1

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

Equipment Items	Qty	Cycle Life	Unit Cost	$/Cycle	Labor Hours
Inst.& Control System					
Manifolding					
Equilibration Vessel					
Wash Vessel					
Eluent Vessel					
Regenerate Vessel					
Storage Vessel					
Waste Vessel(1)					
Product Vessel					
Waste Vessel(2)					
22 Sterile Filtration					
MF Wash Vessel					
Pump					
Filter Holder					
Manifolding					
Instrumentation					
MF Flush Vessel					
MF Prime Vessel					
MF Filtrate Vessel					
MF Wash Vessel					

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FIG. 64Z-2

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

	Seals							Belts	
	Materials					Labor		Materials	
$/Cycle	Item No.	Qty	Cycle Life	Unit Cost	$/Cycle	Hours	$/Cycle	Item No.	Qty
$/Cycle	Item No.	Qty	Cycle Life	Unit Cost	$/Cycle	Hours	$/Cycle	Item No.	Qty

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FIG. 64AA-1

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

Equipment Items	Cycle Life	Unit Cost	$/Cycle	Labor Hours
Inst.& Control System				
Manifolding				
Equilibration Vessel				
Wash Vessel				
Eluent Vessel				
Regenerate Vessel				
Storage Vessel				
Waste Vessel(1)				
Product Vessel				
Waste Vessel(2)				
22 Sterile Filtration				
MF Wash Vessel				
Pump				
Filter Holder				
Manifolding				
Instrumentation				
MF Flush Vessel				
MF Prime Vessel				
MF Filtrate Vessel				
MF Wash Vessel				

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FIG. 64AA-2

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

	Shafts							Lubricant		
	Materials					Labor		Materials		
$/Cycle	Item No.	Qty	Cycle Life	Unit Cost	$/Cycle	Hours	$/Cycle	Item No.	Qty	Cycle Life

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FIG. 64AB-1

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

Equipment Items			Labor
	Unit Cost	$/Cycle	Hours
Inst.& Control System			
Manifolding			
Equilibration Vessel			
Wash Vessel			
Eluent Vessel			
Regenerate Vessel			
Storage Vessel			
Waste Vessel(1)			
Product Vessel			
Waste Vessel(2)			
22 Sterile Filtration			
MF Wash Vessel			
Pump			
Filter Holder			
Manifolding			
Instrumentation			
MF Flush Vessel			
MF Prime Vessel			
MF Filtrate Vessel			
MF Wash Vessel			

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FIG. 64AB-2

EQUIPMENT MAINTENANCE TABLE-MICROBIAL FERMENTATION

	Thermal Media							
	Materials					Labor		
$/Cycle	Item No.	Qty	Cycle Life	Unit Cost	$/Cycle	Hours	$/Cycle

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FIG. 65A-1

MASTER PROCESS PARAMETERS TABLE-BLOPHARMACEUTICAL

		Group 1			
	Unit Operation Type	Parameter	Soln.		Parameter
T1	Inoculum Prep	Number of Flasks Media Volume/Flask		2 0.25 Liters	Temperature Agitation Duration
T2	Flask Growth	Scale Up Ratio Media Volume/Flask		10 Fold 1.25 L	Temperature Agitation Duration
T3	Fermentation Production	Scale Up Ratio Fermentor Working Volume Antifoam A Antifoam B Base Acid	 S-101 S-102 S-103 S-104 S-105	10 Fold 500 Liters 1 Ml/L 1 Ml/L 5 Ml/L 5 Ml/L	Growth Temperature Agitation Sparge Rate Back Pressure Total Duration
T4	Initial Seeding	Number of Ampules Volume Per Ampule Starting Cell Density Ampule Split Ratio Culture Vessel Type Feed Volume		2 2 Ml 300,000 Cells/Ml 1 Vessels/Ampule Roll. Bot. 100 Ml	Serum Content Feed Rate Days to Confluence
T5	Culture Vessel Split	Vessel Split Ratio New Vessel Type Feed Volume Serum Content		2 RB 100 Ml 2.0% Fetal Bovine Serum	Feed Rate Days to Confluence
T6	Spinner Flask Seeding	Flask Feed Volume Vessel/Flask Ratio uCarrier Density Number of PBS Washes Number of Media Washes No.of Media/Serum Washes		4 Liters 0.1 L Cells/L Flask 5 Gm/Liter 2 1 2 FBS	Serum Content Feed Rate Days to Confluence
T7	Biosynthesis Bioreactor Preparation (Stirred Tank Reactor)	Reactor Feed Volume Spinner/Reactor Ratio uCarrier Density Number of PBS Washes Number of Media Washes No.of Media/Serum Washes		500 Liters 8.3 5 Gm/Liter 2 1 2	Serum Content Feed Rate Days to Confluence Serum Free Media Washes
T8	Biosynthesis Bioreactor Preparation (Hollow Fiber Reactor)	Reactor Feed Volume Number of PBS Washes Number of Media Washes No.of Media/Serum Washes Serum Content		100 Liters 2 2 2 2.0% Fetal Bovine Serum	Number of Reactors Feed Rate Days to Confluence
T9	Biosynthesis Bioreactor Preparation (Fluidized Bed Reactor)	Reactor Feed Volume uCarrier Density Number of PBS Washes Number of Media Washes No.of Media/Serum Washes Serum Content		Liters Gms/L	Number of Reactors Feed Rate Days to Confluence
T10	Initial seeding	Number of Ampules Volume Per Ampule Starting Cell Density Ampule Split Ratio		2 2 Ml 300,000 Cells/Ml 1 Vessels/Ampule	Serum Content Feed Rate Days to Confluence

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FIG. 65A-2

MASTER PROCESS PARAMETERS TABLE-BLOPHARMACEUTICAL

Group 2			Group 3		
	Soln.		Parameter	Soln.	
		37 C 200 RPM 18 Hours	Final OD		12
		37 C 200 Hours 18 RPM	Final OD		12
		37 Hours 1 HP/100L 1.5 VVM 5 PSIG 21 Hrs	Final OD Dry Cell Mass Product Concentration CIP		12 9.96 Gms TDCM/L 0.3 Gms Product/L Y
		2.0% Fetal Bovine Serum 1 Feed per vessel per 2 Days 2 Days	Amplification Factor		100%
		1 Feed per vessel per 2 Days 2 Days	Amplification Factor		100%
		2.0% Fetal Bovine Serum 1 Feed per vessel per 2 Days 2 Days	Amplification Factor		100%
		2.0% Fetal Bovine Serum 1 Feed per vessel per 2 Days 10 Days 2	Product Concentration Total Protein Concen.		2500% Mg Prod/L 0.125 Mg TP/MI
		1 1 Feed per vessel per 1 Days 10 Days	Harvest Volume Product Concentration Total Protein Concen.		500% Liters 25 Mg Prod/L 0.125 Mg TP/MI
		1 1 Feed per vessel per 1 Days 10 Days	Product Concentration Total Protein Concen.		2500% Mg Prod/L 0.125 Mg TP/MI
		2.0% Fetal Bovine Serum 1 Feed per vessel per 2 Days 2 Days	Amplification Factor		100%

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FIG. 65B-1

MASTER PROCESS PARAMETERS TABLE-BIOPHARMACEUTICAL

		Group 1			
	Unit Operation Type	Parameter	Soln.		Parameter
		Culture Vessel Type Feed Volume		Roll. Bot. 100 Ml	PBS Washes Trypsin Wash
T11	Culture Vessel Split	Vessel Split Ratio New Vessel Type Feed Volume Serum Content		2 RB 100 Ml 2.0% Fetal Bovine Serum	Feed Rate Days to Confluence PBS Washes Trypsin Wash
T12	Spinner Flask Split	Flask Feed Volume Vessel/Flask Ratio uCarrier Density Number of PBS Washes Number of Media Washes No. of Media/Serum Washes		4 Liters 0.1 L Cells/L Flask 5 Gm/Liter 2 1 2	Serum Content Feed Rate Days to Confluence
T13	Biosynthesis Bioreactor Preparation (Stirred Tank Reactor)	Reactor Feed Volume Spinner/Reactor Ratio uCarrier Density Number of PBS Washes Number of Media Washes No. of Media/Serum Washes		500 Liters 8.3 5 Gm/Liter 2 1 2	Serum Content Feed Rate Days to Confluence Serum Free Media Washes
T14	Biosynthesis Bioreactor Preparation (Fluidized Bed Reactor)	Reactor Feed Volume uCarrier Density Number of PBS Washes Number of Media Washes No. of Media/Serum Washes Serum Content		Liters Gms/L	Number of Reactors Feed Rate Days to Confluence
T15	Intial Coupling	Flask Feed Volume Vessel/Flask Ratio uCarrier Density Number of PBS Washes Number of Media Washes No.of Media/Serum Washes		4 Liters 0.1 L Cells/L Flask 5 Gm/Liter 2 1 2 FBS	Serum Content Feed Rate Days to Confluence
T16	Additional Coupling	Reactor Feed Volume Spinner/Reactor Ratio uCarrier Density Number of PBS Washes Number of Media Washes No.of Media/Serum Washes		500 Liters 8.3 5 Gm/Liter 2 1 2	Serum Content Feed Rate Days to Confluence Serum Free Media Washes
T17	Peptide Cleavage	Reactor Feed Volume Number of PBS Washes Number of Media Washes No.of Media/Serum Washes Serum Content		100 Liters 2 2 2 2.0% Fetal Bovine Serum	Number of Reactors Feed Rate Days to Confluence
T18	Tissue Thawing	Crude Product Yield Environmental Temperature Thaw Duration		25 Gm Crude Prod./Kg Tissue 25 C 16 Hours	Contaminant Protein Conc.
T19	Homogenization	Crude Product Yield Liquid/Solid Ratio Homogenization Temp. Homogenizer Type Energy Input Duration		25 Gm Crude Prod./Kg Tissue 10 L Solution/Kg Tissue 4 C RS 200 HP/100L/Hr 4 Hours	Contaminant Protein Conc.
T20	Liquid Thawing				

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FIG. 65B-2

MASTER PROCESS PARAMETERS TABLE-BLOPHARMACEUTICAL

Group 2			Group 3		
	Soln.		Parameter	Soln.	
		200 MI 100 MI			
		1 Feed per vessel per 2 Days 2 Days 200 MI 100 MI	Amplification Factor		100%
		2.0% Fetal Bovine Serum 1 Feed per vessel per 2 Days 2 Days	Amplification Factor		100%
		2.0% Fetal Bovine Serum 1 Feed per vessel per 2 Days 10 Days 2 Days	Product Concentration Total Protein Concen.		2500% Mg Prod/L 0.125 Mg TP/MI
		1 1 Feed per vessel per 1 Days 10 Days	Product Concentration Total Protein Concen.		2500% Mg Prod/L 0.125 Mg TP/MI
		2.0% Fetal Bovine Serum 1 Feed per vessel per 2 Days 2 Days	Amplification Factor		100%
		2.0% Fetal Bovine Serum 1 Feed per vessel per 2 Days 10 Days 2	Product Concentration Total Protein Concen.		2500% Mg Prod/L 0.125 Mg TP/MI
		1 1 Feed per vessel per 1 Days 10 Days	Harvest Volume Product Concentration Total Protein Concen.		500% Liters 25 Mg Prod/L 0.125 Mg TP/MI
		100 Gm/L	Temperature Regulation CIP SIP		Y Y Y
		100 Gm/L	Temperature Regulation CIP SIP		Y Y Y
			Amplification Factor		100%

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FIG. 65C-1

MASTER PROCESS PARAMETERS TABLE-BLOPHARMACEUTICAL

	Unit Operation Type	Group 1			
		Parameter	Soln.		Parameter
T21	Product Ppt by Solids	Reagent Concentration		1 M	Kgms of Reagent/Liters Product Temperature Addition Time Additional Mix Time
T22	Product Ppt by Liquids	Reagent Concentration		1 M	Liters Reagent/Liters Product Temperature Addition Time Additional Mix Time
T23	Contaminant Ppt by Solids	Reagent Concentration		1 M	Kgms of Reagent/Liters Product Temperature Addition Time Additional Mix Time
T24	Contaminant Ppt by Liquids	Reagent Concentration		1 M	Liters Reagent/Liters Product Temperature Addition Time Additional Mix Time
T25	Solids Harvest Tangential Flow MF	Porosity Average Flux Rate Total Throughput Filtration Time		0.2 Micron 11 L/SF/HR at 40 Psig at 4 C 400 Liters/SF 1 HR	Flush Prime Concentration Factor Wash Regenerate Store
T26	Continuous Centrifugation Solids Harvest	System Void Volume		5 Liters	RCF Time Volume Reduction Wash Volume
T27	Continuous Centrifugation Supernatant Harvest	System Void Volume		6 Liters	RCF Time Volume Reduction Wash Volume
T28	Dilution	System Void Volume		6 Liters	RCF Time Volume Reduction Wash Volume
T29	Batch Centrifugation Solids Harvest	System Void Volume		6 Liters	RCF Time Volume Reduction Wash Volume

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FIG. 65C-2

MASTER PROCESS PARAMETERS TABLE-BIOPHARMACEUTICAL

Group 2			Group 3		
	Soln.		Parameter	Soln.	
		0.25 Kg/L 4 C 0.5 Hours 2 Hours	Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		95% 95% Y Y Y
		0.25 L/L 4 C 0.5 Hours 2 Hours	Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		95% 95% Y Y Y
		0.25 Kg/L 4 C 0.5 Hours 2 Hours	Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		95% 95% Y Y Y
		0.25 L/L 4 C 0.5 Hours 2 Hours	Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		95% 95% Y Y Y
		2 L/SF 2 L/SF 10 Fold 0.5 L/SF 1 L/SF 2 L/SF	Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		95% 95% Y Y Y
		10,000 X G 60 Minutes 30 X Vol. Reduction 0.2 X System Void Volume	Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		95% 95% Y Y Y
		10,000 X G 30 Minutes 0.062 X Vol. Reduction 1.5 X System Void Volume	Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		85% 0.3 Y Y Y
		10,000 X G 30 Minutes 16 X Vol. Reduction 1.5 X System Void Volume	Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		95% 0.95 Y Y Y
		10,000 X G 30 Minutes 16 X Vol. Reduction 1.5 X System Void Volume	Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP		95% 0.95 Y Y

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FIG. 65D-1

MASTER PROCESS PARAMETERS TABLE-BLOPHARMACEUTICAL

		Group 1			
	Unit Operation Type	Parameter	Soln.		Parameter
T30	Batch Centrifugation Supernatent Harvest	System Void Volume		6 Liters	RCF Time Volume Reduction Wash Volume
T31	Cell Disruption High Press. Homogen.	Product Temperature Utility Temperature Void Volume		8 C 2 C 5 Liter	Number of Passes Pressure Flow Rate Temperature Increase
T32	Cell Disruption Bead Mill	Number of Passes Bead Size Void Volume Flow Rate		2 0.5 LPM	
T33	Cell Disruption Chemical Lysis	Reagent Temperature Exposure Time		0.5 M NaOH 4 C 2 Hours	Liters Reagent/Gm Product Titration
T34	Microfiltration Tangential Flow	Porosity Average Flux Rate Total Throughput Filtration Time		0.2 Micron 50 L/SF/HR at 40 Psig at 4 C 400 Liters/SF 2 HR	Flush Prime Wash Solids Regenerate Store
T35	Microfiltration Dead End	Porosity Average Flux Rate Total Throughput Filtration Time		0.2 Micron 50 L/SF/HR at 40 Psig at 4 C 400 Liters/SF 0.5 HR	Flush Prime Wash Solids Regenerate Store
T36	Ultrafiltration Concentration/Dilution	Porosity Average Flux Rate Concentration Time		60 K NMWL 3 L/SF/HR at 40 Psig at 4 C 2 HR	Flush Prime Wash Dilute Concentrate Solids Regenerate
T37	Ultrafiltration Flow Dialysis	Porosity Average Flux Rate Dialysis Time		60 K NMWL 3 L/SF/HR at 40 Psig at 4 C 2 HR	Flush Prime Dialysis Buffer Wash Solids Regenerate
T38	Prod.Ads.Chromatography HPLC	Column Capacity Column Oversize Factor Column Aspect Ratio Max. Linear Velocity		10 MG Prod./Ml Of Packing 1.5 Fold 0.37 H/D 100 Cm/Hr at 45 Psig and 4 C	Column Equilibration Column Wash Column Elute A Column Elute B Column Regenerate Column Store
T39	Prod.Ads.Chromatography HPLC	Column Capacity Column Oversize Factor		10 MG Prod./Ml Of Packing 1.5 Fold	Column Equilibration Column Wash

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(As Amended)

FIG. 65D-2

MASTER PROCESS PARAMETERS TABLE-BLOPHARMACEUTICAL

Group 2			Group 3		
	Soln.		Parameter	Soln.	
			SIP		Y
		10,000 XG 30 Minutes 16 X Vol.Reduction 1.5 X System Void Volume	Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		95% 0.95 Y Y Y
		6 Times 12,000 PSI 5 LPM 1.8 Degrees C/1,000 PSI	Rinse Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		500% Void Volumes 95% 95% Y Y Y
			Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		95% Y Y Y
		0.4 L/Gm 0 MI/Liter	Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		95% Y Y Y
		2.00 L/SF 2.00 L/SF 0.50 L/SF 0.30% Of Product Solution 1.00 L/SF 2.00 L/SF	Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		95% 95% Y Y Y
		0 L/SF 0 L/SF 0.50 L/SF 0.003 Of Product Solution 1 L/SF 2 L/SF	Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		95% 0.95% N N N
		2.00 L/SF 2.00 L/SF 0.50 L/SF 10.0 Fold 0.30% Of Product Solution 1.00 L/SF	Store Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		2.00 L/SF 95% 95% Y Y Y
		2 L/SF 2.00 L/SF 5.0 X Feed Stream Volume 0.50 L/SF 0.30% Of Product Solution 1.00 L/SF	Store Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		200% L/SF 95% 95% Y Y Y
		5 Column Volumes 3 Column Volumes 3 Column Volumes 0 Column Volumes 1 Column Volumes 2 Column Volumes	Prod.Elution Volume Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		80% 95% 95% N Y Y
		5 Column Volumes 3 Column Volumes	Prod.Elution Volume Step Recovery of Product		80% 95%

FIG. 65E-1

MASTER PROCESS PARAMETERS TABLE-BIOPHARMACEUTICAL

	Unit Operation Type	Parameter	Soln.		Parameter
		Column Aspect Ratio Max. Linear Velocity		0.37 H/D 100 Cm/Hr at 45 Psig and 4 C	Column Elute A Column Elute B Column Regenerate Column Store
T40	Prod.Ads.Chromatography LPLC	Column Capacity Column Oversize Factor Column Aspect Ratio Max. Linear Velocity		10 MG Prod./Ml Of Packing 1.5 Fold 0.37 H/D 100 Cm/Hr at 45 Psig and 4 C	Column Equilibration Column Wash Column Elute A Column Elute B Column Regenerate Column Store
T41	Cont.Ads.Chromatography HPLC	Column Capacity Column Oversize Factor Column Aspect Ratio Max. Linear Velocity		30 MG Cont./Ml Of Packing 1.5 Fold 0.37 H/D 100 Cm/Hr at 45 Psig and 4 C	Column Equilibration Column Wash Column Elute A Column Elute B Column Regenerate Column Store
T42	Cont.Ads.Chromatography MPLC	Column Capacity Column Oversize Factor Column Aspect Ratio Max. Linear Velocity		10 MG Cont./Ml Of Packing 1.5 Fold 0.37 H/D 100 Cm/Hr at 45 Psig and 400% C	Column Equilibration Column Wash Column Elute A Column Elute B Column Regenerate Column Store
T43	Cont.Ads.Chromatography LPLC	Column Capacity Column Oversize Factor Column Aspect Ratio Max. Linear Velocity		10 MG Cont./Ml Of Packing 1.5 Fold 0.37 H/D 100 Cm/Hr at 45 Psig and 4 C	Column Equilibration Column Wash Column Elute A Column Elute B Column Regenerate Column Store
T44	Size Excl.Chromatography HPLC	Load Capacity Length Max. Linear Velocity Void Volume		5% of Total Column Volume 100 Cm 100 Cm/Hr at 45 Psig and 4 C 25% Column Volume	Column Equilibration Column Wash Column Regenerate Column Store
T45	Size Excl.Chromatography MPLC	Load Capacity Length Max. Linear Velocity Void Volume		5% of Total Column Volume 100 Cm 100 Cm/Hr at 45 Psig and 4 C 25% Column Volume	Column Equilibration Column Wash Column Regenerate Column Store
T46	Size Excl.Chromatography LPLC	Load Capacity Length Max. Linear Velocity Void Volume		5% of Total Column Volume 100 Cm 100 Cm/Hr at 45 Psig and 4 C 25% Column Volume	Column Equilibration Column Wash Column Regenerate Column Store
T47	Dilution	Dilution Factor		3 Liters/Liter	Dilution Time Additional Mix Time
T48	Resolubilization	Reagent/Product Ratio Dissolution Time Additional Mix Time		0 L/Kg Product 0.50 Hours 0.50 Hours	Reagent 1 Concentration

FIG. 65E-2

MASTER PROCESS PARAMETERS TABLE-BLOPHARMACEUTICAL

Group 2		Group 3		
Soln.		Parameter	Soln.	
	3 Column Volumes	Step Recovery of T.P.		95%
	0 Column Volumes	Temperature Regulation		N
	1 Column Volumes	CIP		Y
	2 Column Volumes	SIP		Y
	5 Column Volumes	Prod. Elution Volume		42%
	3 Column Volumes	Step Recovery of Product		95%
	3 Column Volumes	Step Recovery of T.P.		95%
	2 Column Volumes	Temperature Regulation		N
	1 Column Volumes	CIP		Y
	2 Column Volumes	SIP		Y
	5 Column Volumes	Prod. Elution Volume		42%
	3 Column Volumes	Step Recovery of Product		95%
	3 Column Volumes	Step Recovery of T.P.		95%
	2 Column Volumes	Temperature Regulation		N
	1 Column Volumes	CIP		Y
	2 Column Volumes	SIP		Y
	5 Column Volumes	Prod. Elution Volume		42%
	3 Column Volumes	Step Recovery of Product		95%
	3 Column Volumes	Step Recovery of T.P.		95%
	2 Column Volumes	Temperature Regulation		N
	1 Column Volumes	CIP		Y
	2 Column Volumes	SIP		Y
	5 Column Volumes	Prod. Elution Volume		42% Columns Volumes
	3 Column Volumes	Step Recovery of Product		95%
	3 Column Volumes	Step Recovery of T.P.		95%
	2 Column Volumes	Temperature Regulation		N
	1 Column Volumes	CIP		Y
	2 Column Volumes	SIP		Y
	4 Column Volumes	Prod. Elution Volume		42% Columns Volumes
	1 Column Volumes	Step Recovery of Product		95%
	1 Column Volumes	Step Recovery of T.P.		95%
	2 Column Volumes	Temperature Regulation		N
		CIP		Y
		SIP		Y
	4 Column Volumes	Prod. Elution Volume		42% Columns Volumes
	1 Column Volumes	Step Recovery of Product		95%
	1 Column Volumes	Step Recovery of T.P.		95%
	2 Column Volumes	Temperature Regulation		N
		CIP		Y
		SIP		Y
	4 Column Volumes	Prod. Elution Volume		42% Columns Volumes
	1 Column Volumes	Step Recovery of Product		95%
	1 Column Volumes	Step Recovery of T.P.		95%
	2 Column Volumes	Temperature Regulation		N
		CIP		Y
		SIP		Y
	0.5 Hours	Step Recovery of Product		95%
	1 Hours	Step Recovery of T.P.		95%
		Temperature Regulation		Y
		CIP		Y
		SIP		Y
	Water	Step Recovery of Product		95%
	Dist.	Step Recovery of T.P.		95%
		Temperature Regulation		Y
		CIP		Y
		SIP		Y

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Inventor: Peter G. BROWN; Tel. No.: 202-371-2600
For: **Method for Scheduling Solution Preparation in Biopharmaceutical Batch Process Manufacturing**
(As Amended)

FIG. 65F-1

MASTER PROCESS PARAMETERS TABLE-BLOPHARMACEUTICAL

		Group 1			
	Unit Operation Type	Parameter	Soln.		Parameter
T49	Enzymatic Modification	Enzyme to Product Ratio Enzyme Concentration Reaction Temp. Reaction Duration		0.084 Liters of Enzyme Stock Per Liter of Start Proc. Vol. 2 Mg/Ml 37 Degrees C 30 Minutes 100%	Titration Solution-1 Titration Solution-2 Neutralization
T50	Lyophilization	Product Capacity/Load Product Unit Size		8 Units 100 Grams/Unit	Lyophilization Time Product Weight Reduction
T51	Heat Exchange	Process Initial Temp. Process Final Temp Utility Initial Temp. Utility Final Temp. Process Specific Heat Design Type(P.T.C)		98.6 Degrees C 39.2 Degrees C 34 Degree C 5 Degrees C 38.6 K BTU/Hr P	Exposure Time
T52	Storage				
T53	Fermentation Seed	Scale Up Ratio Fermentor Working Volume Antifoam A Antifoam B Base Acid		10 Fold 50 Liters 1 Ml/L 1 Ml/L 5 Ml/L 5 Ml/L	Growth Temperature Agitation Sparge Rate Back Pressure Total Duration
54	Initial Seeding	Flask Feed Volume Spinner Split Ratio uCarrier Density Number of PBS Washes Number of Media Washes No. of Media/Serum Washes		12 Liters 4 5 Gm/Liter 2 1 2 FBS	Serum Content Feed Rate Days to Confluence
55	Culture Vessel Split	Flask Feed Volume Spinner Split Ratio uCarrier Density Number of PBS Washes Number of Media Washes No. of Media/Serum Washes		12 Liters 4 5 Gm/Liter 2 1 2 FBS	Serum Content Feed Rate Days to Confluence
56	Culture Flask Split				
57	Stirred Tank Reactor				
58	Fluidized Bed Reactor	Process Initial Temp. Process Final Temp Utility Initial Temp		37 Degree C 4 Degree C 2 Degree C	Exposure Time

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FIG. 65F-2

MASTER PROCESS PARAMETERS TABLE-BLOPHARMACEUTICAL

Group 2		Group 3		
Soln.		Parameter	Soln.	
	0.067 L/L Process 0.02 L/L Process 0.57 L/L Process	Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		95% 95% Y Y Y
	18 Hours 0.95	Step Recovery of Product Step Recovery of T.P. CIP SIP		95% 95% Y Y Y
	1 Hours	Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		100% 100% Y Y Y
		Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		95% 95% Y Y Y
	37 Hours 1 HP/100L 1.5 VVM 5 PSIG 21 Hrs	Final OD CIP		12 Y
	2% FBS 1 Feed per vessel per 2 Days 2 Days	Amplification Factor		1
	2% FBS 1 Feed per vessel per 2 Days 2 Days	Amplification Factor		1
		Step Recovery of Product Step Recovery of T.P. CIP SIP		0.95 95% Y Y Y
	50% Hours	Step Recovery of Product Step Recovery of T.P.		0.95 100%

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(As Amended)

FIG. 65G-1

MASTER PROCESS PARAMETERS TABLE-BIOPHARMACEUTICAL

	Unit Operation Type	Group 1			
		Parameter	Soln.		Parameter
		Utility Final Temp. Process Specific Heat Design Type(P.T.C)		5 Degrees C 12 K BTU/Hr P	
59	Liquid/Liquid Extraction	Liquid/Liquid Ratio Extraction Temperature Addition Duration Additional Mix Duration Mix Energy		1 L Extraction/L Product 4 C 0.5 Hours 4 Hours 0.3 HP/100 L	Phase Separation Time Product Phase(Top/Bottom) Harvest Time
60	Solid/Liquid Extraction	Liquid/Liquid Ratio Extraction Temperature Duration Mix Energy		1 L Extraction/L Product 4 C 4 Hours 0.3 HP/100 L	Phase Separation Time Product Phase(Top/Bottom) Harvest Time

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FIG. 65G-2

MASTER PROCESS PARAMETERS TABLE-BLOPHARMACEUTICAL

Group 2			Group 3		
	Soln.		Parameter	Soln.	
			Temperature Regulation CIP SIP		Y Y Y
		1600% Hours Top 0.5 Hours	Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		0.9 50% Y Y Y
		1600% Hours Top 0.5 Hours	Step Recovery of Product Step Recovery of T.P. Temperature Regulation CIP SIP		0.9 50% Y Y Y